CHEMICAL INVESTIGATIONS IN ALICYCLIC SYSTEMS WITH SPECIAL REFERENCE TO STEROIDS

RESUME

THESIS SUBMITTED FOR THE DEGREE OF

Doctor of Philosophy

IN

CHEMISTRY

TO

THE ALIGARH MUSLIM UNIVERSITY, ALIGARH

S. KALBEY RAZA

DEPARTMENT OF CHEMISTRY
A. M. U. ALIGARH, 202001

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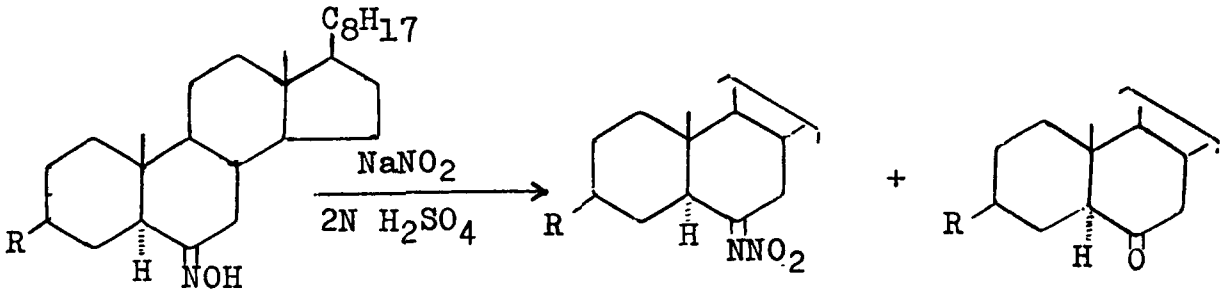
PART - ONE

Nitrosation of Steroidal Ketoximes

The fact, that no significant work has been done on the nitrosation of steroidal ketoximes, prompted us to undertake the nitrosation of some of the easily accessible steroidal ketoximes in the cholestane series. The ketoximes examined were 6-oximino-5α-cholestane (I), 6-oximino-5α-cholestan-3β-yl chloride (II), 6-oximino-5α-cholestan-3β-yl acetate (III), 6-oximino-3α,5-cyclo-5α-cholestane (IV), 3-oximinocholest-4-ene (V), 7-oximinocholest-5-ene (VI), 7-oximinocholest-5-en-3β-yl chloride (VII), 7-oximinocholest-5-en-3β-yl acetate (VIII) and 3,6-dioximino-5α-cholestane (IX).

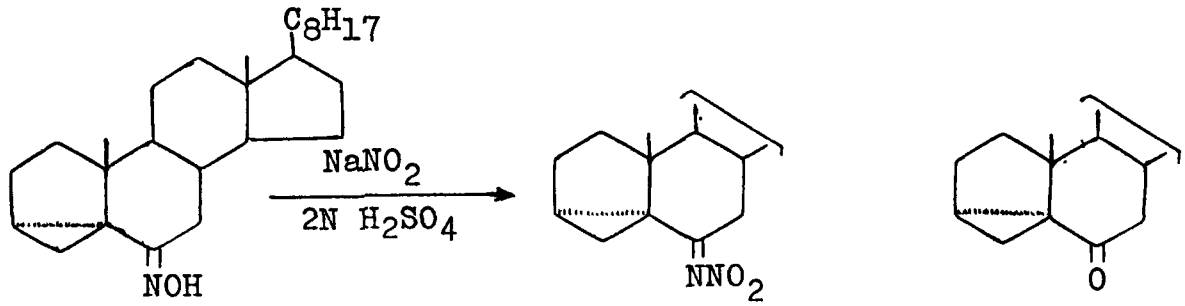
The products obtained, from the nitrosation reaction of the above mentioned steroidal ketoximes, have been characterized on the basis of their spectral properties, chemical transformations and by comparison with the authentic samples where available. The results have been summarized in the following flowsheet.



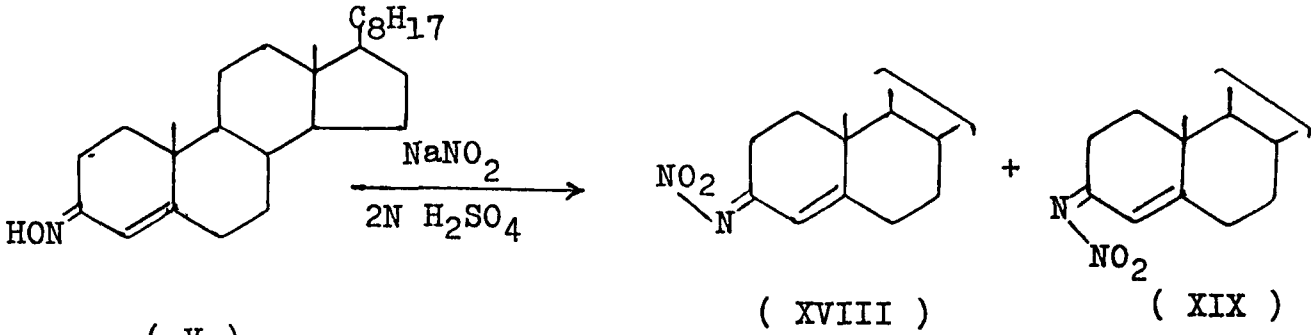
(I) R = H (X) R = H (XI) R = H

(II) R = Cl (XII) R = Cl (XIII) R = Cl

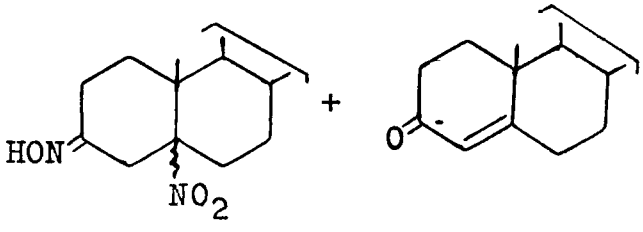
(III) R = OAc (XIV) R = OAc (XV) R = OAc



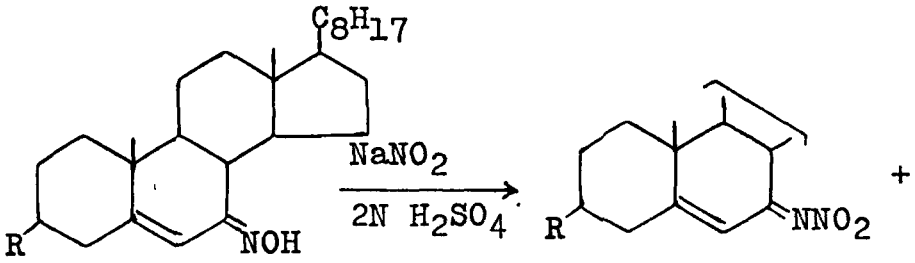
(IV) (XVI) (XVII)



(V) (XVIII) (XIX)



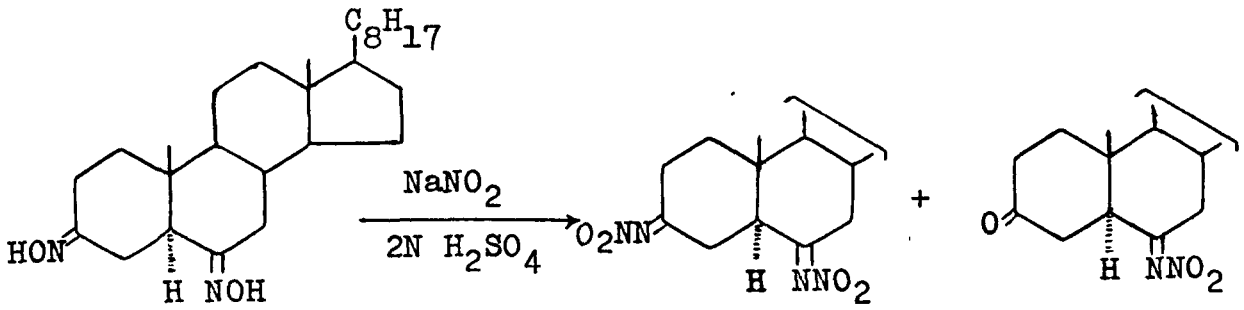
(XX) (XXI)



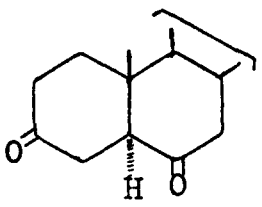
(VI) R = H (XXII) R = H (XXIII) R = H

(VII) R = Cl (XXIV) R = Cl (XXV) R = Cl

(VIII) R = OAc (XXVI) R = OAc (XXVII) R = OAc



(IX) (XXVIII) (XXIX)



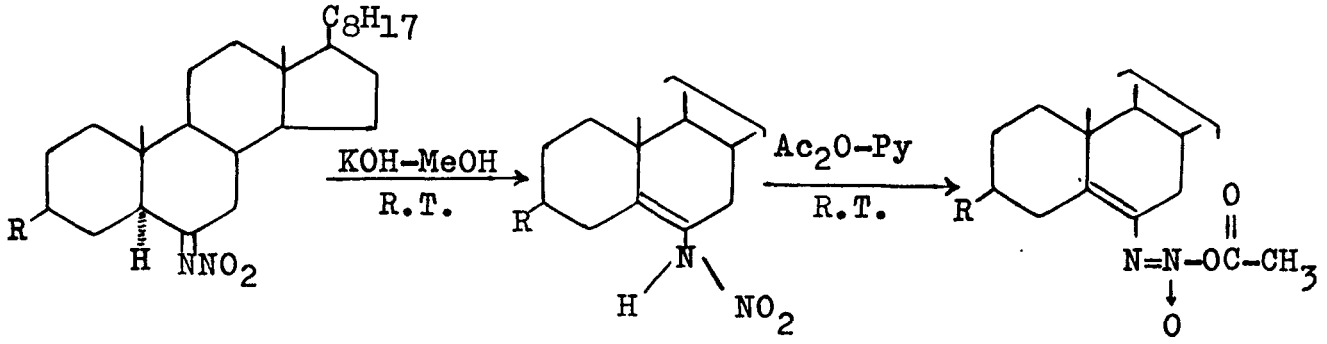
(XXX)

PART - TWO

Transformations of Steroidal Nitrimines

The nitrimines, obtained from the nitrosation reaction of ketoximes, undergo some interesting transformations to give a variety of products. We have therefore, carried out certain reactions of the steroidal nitrimines prepared by us. The transformations undertaken are, (i) isomerization by methanolic potassium hydroxide to give the nitroenamines, (ii) reduction with sodium borohydride in absolute ethanol to give nitroamines and (iii) thermolysis in refluxing xylene to give some interesting steroidal derivatives.

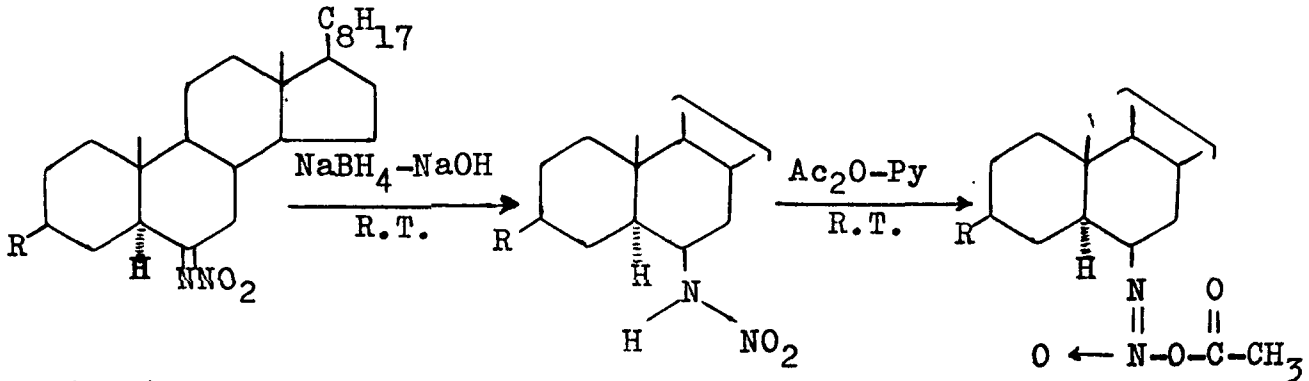
The isomerization of 6-nitrimino-5α-cholestane (X), 6-nitrimino-5α-cholestan-3β-yl chloride (XII) and 6-nitrimino-5α-cholestan-3β-yl acetate (XIV) with methanolic KOH at room temperature furnished their isomeric nitroenamines (XXXI-XXXIII) which were identified on the basis of their spectral properties. The reaction of these nitroenamines with acetic anhydride and pyridine gave their N-oxidoacetate derivatives (XXXIV-XXXVI).



(X)	R = H	(XXXI)	R = H	(XXXIV)	R = H
(XII)	R = Cl	(XXXII)	R = Cl	(XXXV)	R = Cl
(XIV)	R = OAc	(XXXIII)	R = OH	(XXXVI)	R = OH

The reduction of 6-nitrimino-5α-cholestane (X), 6-nitrimino-5α-cholestan-3β-yl chloride (XII), 6-nitrimino-5α-cholestan-3β-yl acetate (XIV) and 7-nitriminocholest-5-en-3β-yl chloride (XXIV) with sodium borohydride in absolute ethanol at room temperature gave their respective N-nitroamines (XXXVII-XL). These nitroamines were characterized on the basis of their spectral properties.

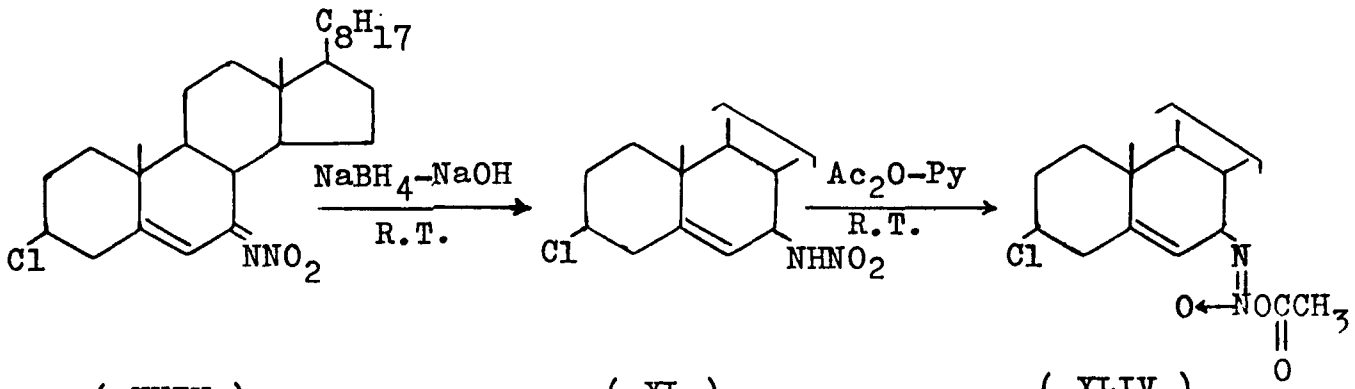
The acetylation of the nitroamines (XXXVII-XL) with acetic anhydride and pyridine at room temperature gave their respective O-acetyl-aci-nitroamines (XLI-XLIV).



(X) R = H
(XII) R = Cl
(XIV) R = OAc

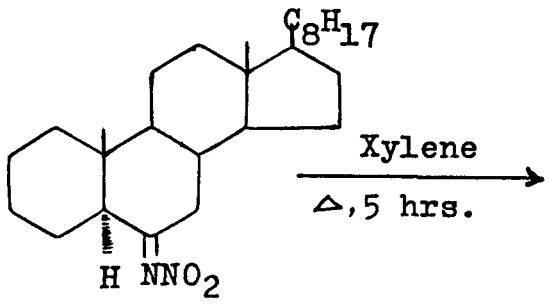
(XXXVII) R = H
(XXXVIII) R = Cl
(XXXIX) R = OH

(XLI) R = H
(XLII) R = Cl
(XLIII) R = OH

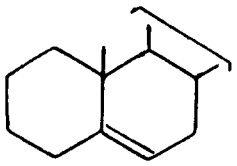


(XXIV) (XL) (XLIV)

The thermolysis of 6-nitrimino-5α-cholestane (X), 6-nitrimino-5α-cholestan-3β-yl acetate (XII) and 7-nitriminocholest-5-en-3β-yl chloride (XXIV) in refluxing xylene resulted in the formation of some interesting steroidal derivatives. The products were identified on the basis of their spectral properties and comparison with authentic samples where available.

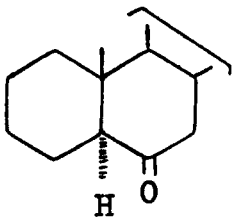


(X)

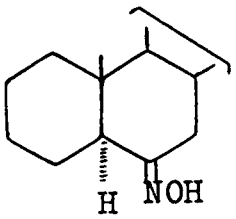


(XLV)

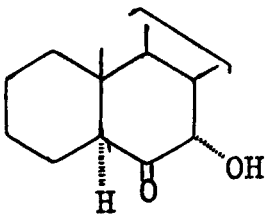
+



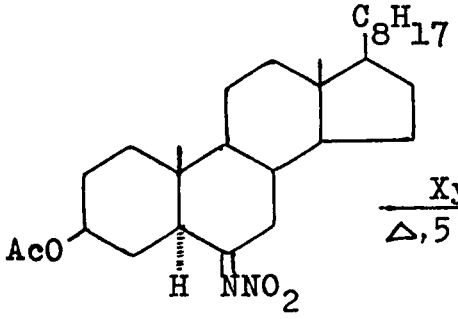
(XI)



(I)

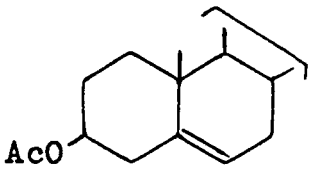


(XLVI)



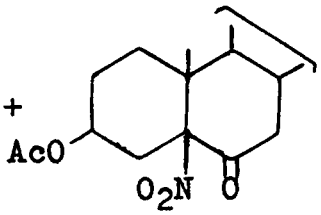
(XIV)

Xylene
△, 5 hrs.



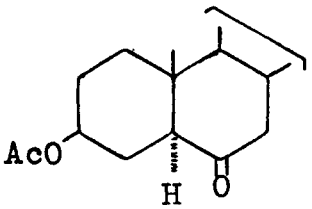
(XLVII)

+



+

(XLVIII)



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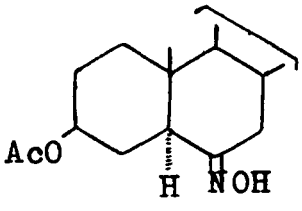
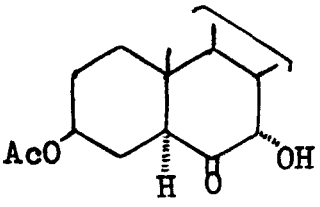
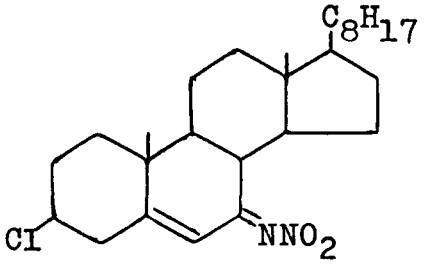


(III)

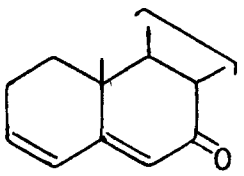


(XLIX)



(XXIV)

Xylene
△, 5 hrs.



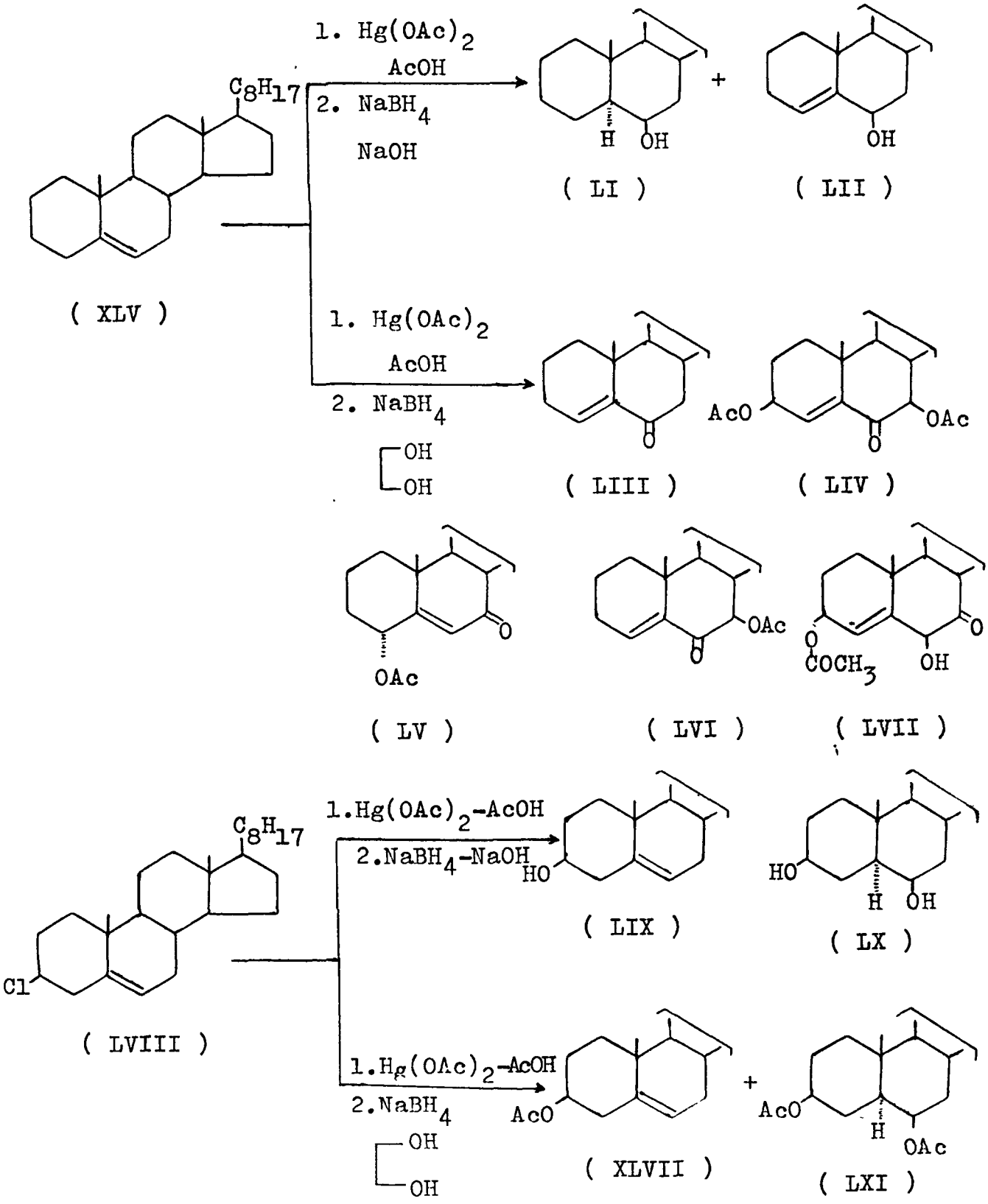
(L)

PART - THREE

A. Oxymercuration-Demercuration of Steroidal Olefins

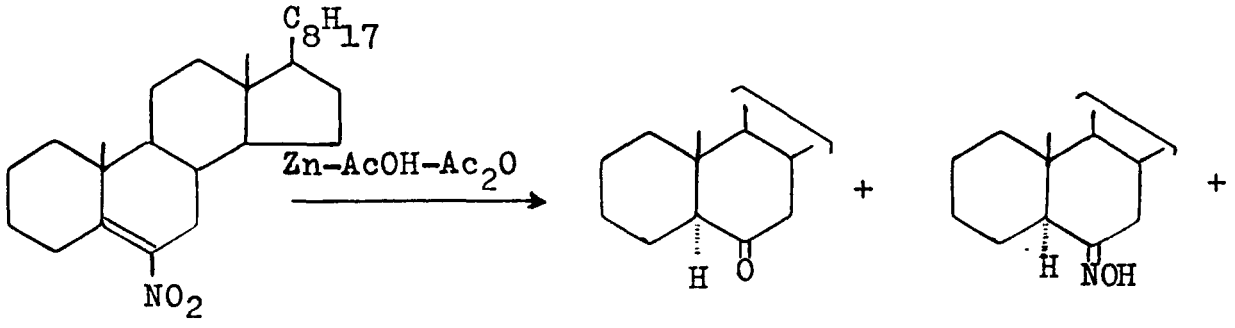
The oxymercuration-demercuration procedure provides a simple and convenient route to the Markownikoff hydration of carbon-carbon double bonds. The stereo- and regioselectivity attached with this reaction and the variations exhibited, particularly in the demercuration of the organomercurial adducts, prompted us to undertake the oxymercuration-demercuration of some of the easily accessible steroidal olefins in the cholestane series. The aim was to prepare some steroidal hydroxy ethers, previously prepared in our laboratory by mixed hydride reduction of cylic ketals, by empolying ethylene glycol and sodium borohydride at the demercuration step.

The oxymercuration of cholest-5-ene (XLV) and cholest-5-en-3β-yl chloride (LVIII) was done with mercuric acetate in acetic acid while the demercuration was affected under different reaction media. The products have been characterized on the basis of their spectral properties, chemical transformations and comparison with authentic samples where available. The results have been summarized in the following flowsheet.

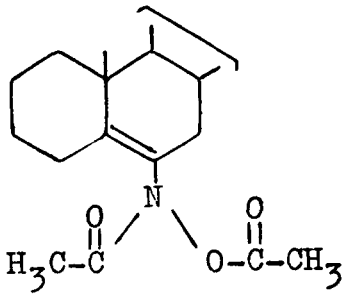

1. Hg(OAc)2
AcOH
2. NaBH4
NaOH
C8H17
H
OH
OH
(XLV)
(LI)
(LII)
1. Hg(OAc)2
AcOH
2. NaBH4
OH
OH
(LIII)
AcO
OAc
(LIV)
OAc
O
(LV)
OAc
O
(LVI)
O
O
COCH3
OH
(LVII)
1.Hg(OAc)2-AcOH
2.NaBH4-NaOH
C8H17
Cl
HO
(LIX)
HO
H
OH
(LX)
(LVIII)
1.Hg(OAc)2-AcOH
2.NaBH4
OH
OH
AcO
(XLVII)
AcO
H
OAc
(LXI)

B. Reduction of Steroidal Nitroolefins with Zn-AcOH Without Water

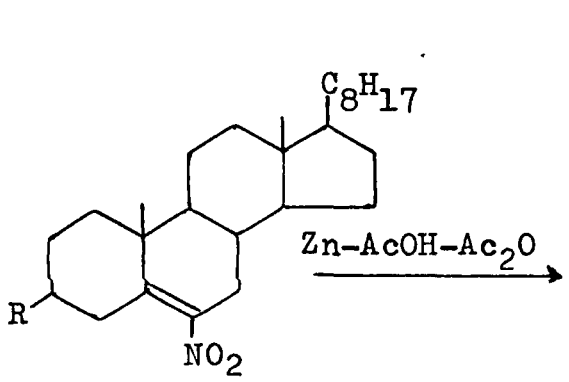
The conversion of nitroolefins into ketones by zinc-acetic acid-water reduction is a well known method. We made an attempt to carry out the reduction of steroidal nitroolefins, such as 6-nitrocholest-5-ene (LXII) and its 3β-chloro (LXIII) and 3β-acetoxy (LXIV) analogues, with zinc-acetic acid without added water in order to screen the intermediate involved in this reduction. We succeeded in isolating some acetylated enamine type of compounds, besides the respective ketones and oximes. The products obtained have been characterized on the basis of their spectral properties and comparison with authentic samples where available. The results have been summarized in the following flowsheet.



(LXII) (XI) (I)

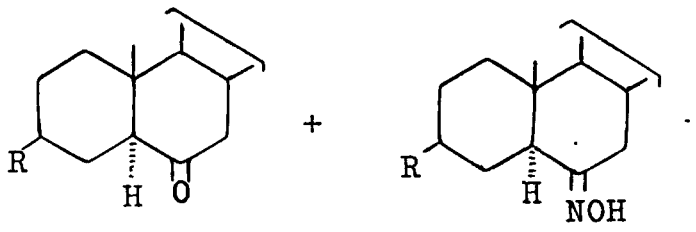


(LXV)



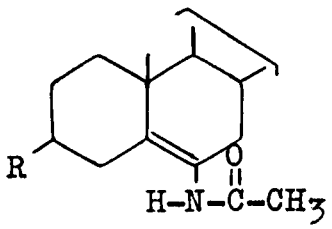
(LXIII) R = Cl

(LXIV) R = OAc



(XII) R = Cl (II) R = Cl

(XV) R = OAc (III) R = OAc



(LXVI) R = Cl

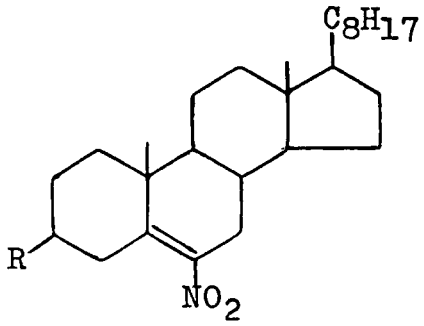
(LXVII) R = OAc

PART - FOUR

Mass Spectral Studies on Steroidal Nitro Compounds

During the last twenty five years or so the mass spectrometry has developed to become a very powerful analytical tool in the characterization of organic compounds. Virtually, every class of organic compounds had been subjected to this study and useful structure-spectra relationships have been established. It was, however, found that no significant studies have been made on the mass spectrometry of steroidal nitro compounds and this prompted us to undertake such studies on some of the

structurally related steroidal nitro compounds. These included the steroidal nitroolefins such as 6-nitrocholest-5-ene (LXII), 6-nitrocholest-5-en-3β-yl chloride (LXIII) and 6-nitrocholest-5-en-3β-yl acetate (LXIV).

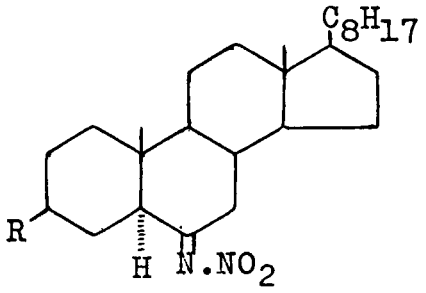


(LXII) R = H

(LXIII) R = Cl

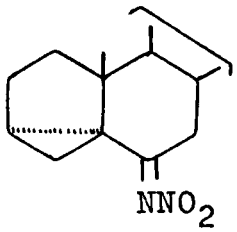
(LXIV) R = OAc

Besides these C-nitrosteroids, we also undertook the mass spectral studies on some N-nitrosteroids (nitrimines) which have been prepared in our laboratory. The nitrimines selected for the study were 6-nitrimino-5α-cholestane (X), 6-nitrimino-5α-cholestan-3β-yl acetate (XIV), 6-nitrimino-3α-5-cyclo-5α-cholestane (XVI), 7-nitriminocholest-5-ene (XXII), 7-nitrimino-cholest-5-en-3β-yl acetate (XXVI) and anti- and syn- forms of 3-nitriminocholest-4-ene (XVIII) and (XIX), respectively.

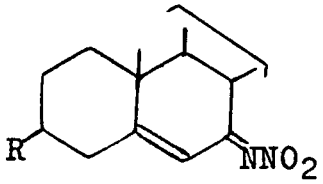


(X) R = H

(XIV) R = OAc

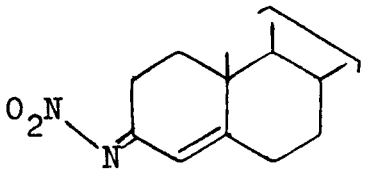


(XVI)

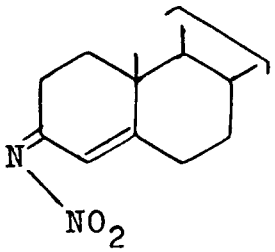


(XXII) R = H

(XXVI) R = OAc



(XVIII)



(XIX)

These studies were undertaken with a view to assess the effect of nitro group and to evaluate the effect of substitution on the fragmentation pattern. An attempt has also been made to visualize that how the fragmentation pattern of N-nitrosteroids differs from that of the C-nitrosterodis.

The proposed fragmentation pathways are supported in some cases by appropriate metastable peaks. The mechanisms suggested are only tentative in the absence of appropriate deuterated analogues and the accurate mass measurements.

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A. M. U. ALIGARH, 202001

July, 1984

Department of Chemistry
Aligarh Muslim University
Aligarh

This is to certify that the work embodied in this thesis is the original work of the candidate accomplished under my supervision. The thesis is suitable for submission for the award of Ph.D. degree in Chemistry.

M.S. Ahmad

(M.S. Ahmad)

Professor of Chemistry

ACKNOWLEDGEMENT

I wish to express my extreme indebtedness to Professor M. Shahabuddin Ahmad for his help, proper guidance, encouragement and unstinted devotion to my work. I am thankful to Professor W. Rahman, Ex-Chairman, Department of Chemistry for providing necessary facilities and to the CSIR, New Delhi, for financial assistance.

I shall be failing in my duty if I do not appreciate the efforts of Dr. M. Mushfiq without whose help and devotion this work should have not assumed the final shape. I also thankfully recognize the efforts of Mr. Tanveer S. Siddiqui who strained himself in drawing the mass spectra. I am thankful to my research colleagues for their cooperation and helpful suggestions. The execution of the uphill task of typing the script by Mr. Mohd. Zubair Siddiqui is gratefully acknowledged.

(S. Kalbey Raza)

C O N T E N T S

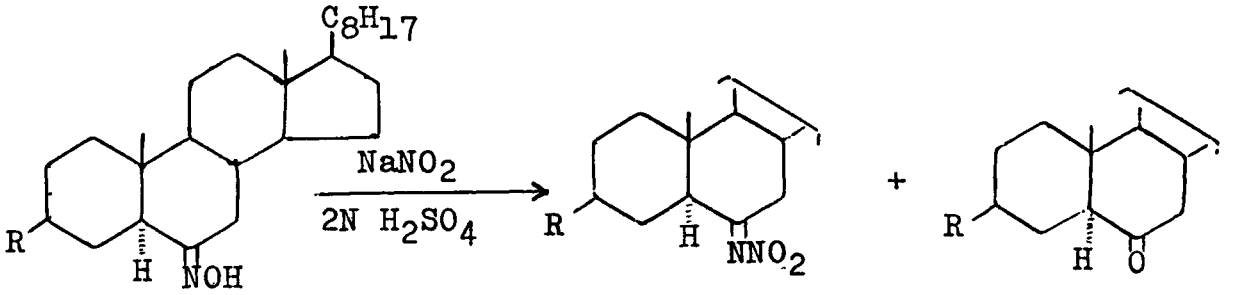
S U M M A R Y

PART - ONE

Nitrosation of Steroidal Ketoximes

The fact, that no significant work has been done on the nitrosation of steroidal ketoximes, prompted us to undertake the nitrosation of some of the easily accessible steroidal ketoximes in the cholestane series. The ketoximes examined were 6-oximino-5α-cholestane (I), 6-oximino-5α-cholestan-3β-yl chloride (II), 6-oximino-5α-cholestan-3β-yl acetate (III), 6-oximino-3α,5-cyclo-5α-cholestane (IV), 3-oximinocholest-4-ene (V), 7-oximinocholest-5-ene (VI), 7-oximinocholest-5-en-3β-yl chloride (VII), 7-oximinocholest-5-en-3β-yl acetate (VIII) and 3,6-dioximino-5α-cholestane (IX).

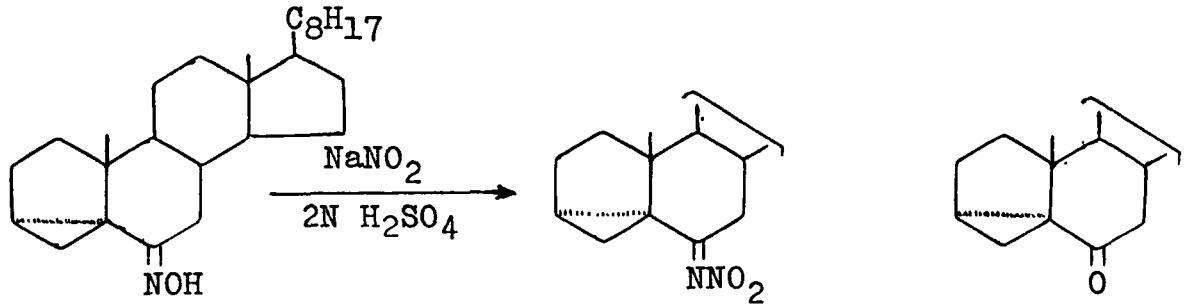
The products obtained, from the nitrosation reaction of the above mentioned steroidal ketoximes, have been characterized on the basis of their spectral properties, chemical transformations and by comparison with the authentic samples where available. The results have been summarized in the following flowsheet.



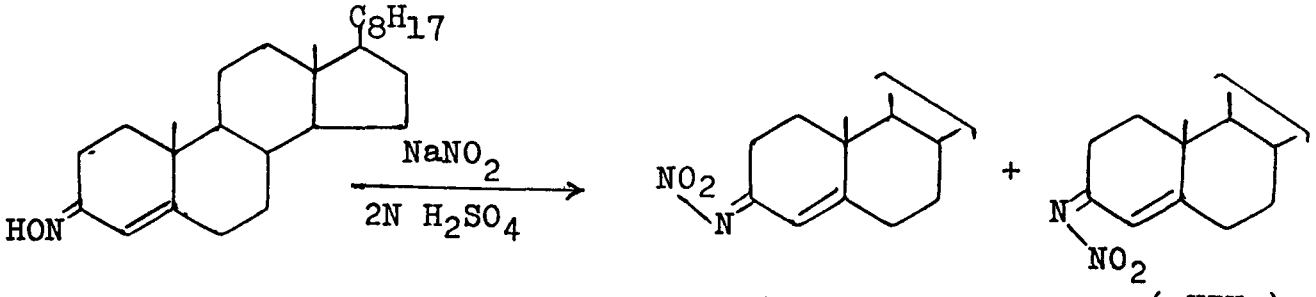
(I) R = H (X) R = H (XI) R = H

(II) R = Cl (XII) R = Cl (XIII) R = Cl

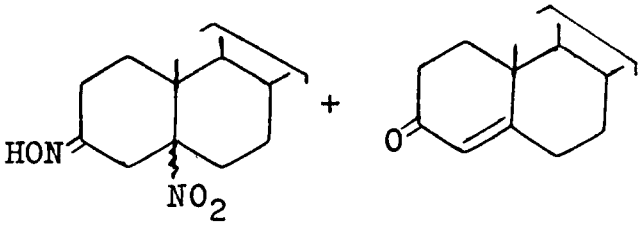
(III) R = OAc (XIV) R = OAc (XV) R = OAc



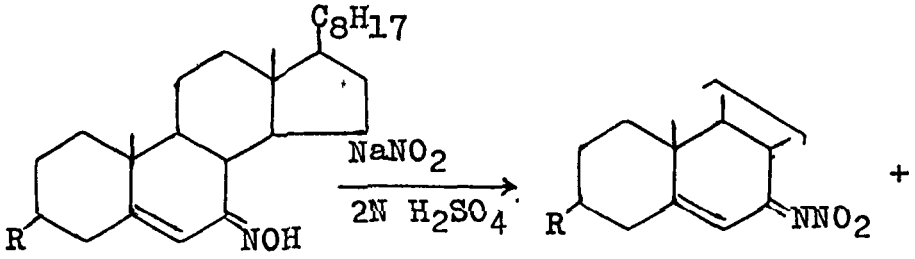
(IV) (XVI) (XVII)



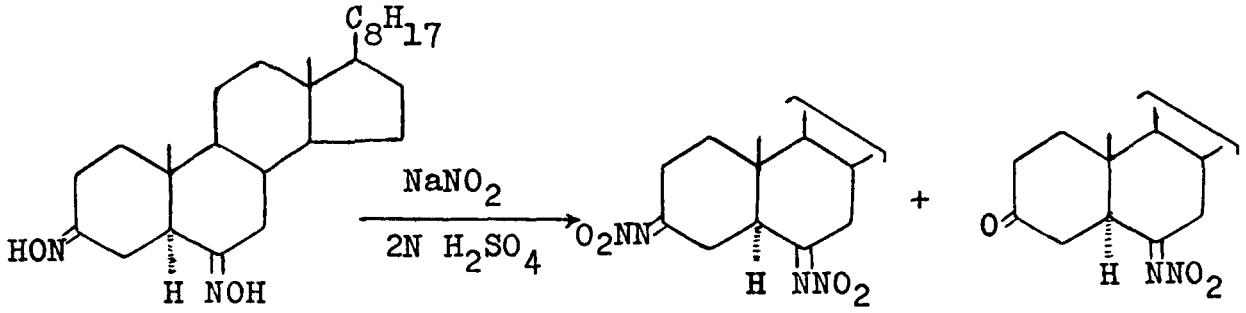
(V) (XVIII) (XIX)



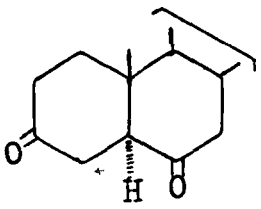
(XX) (XXI)



(VI)	R = H	(XXII)	R = H	(XXIII)	R = H
(VII)	R = Cl	(XXIV)	R = Cl	(XXV)	R = Cl
(VIII)	R = OAc	(XXVI)	R = OAc	(XXVII)	R = OAc



(IX) (XXVIII) (XXIX)



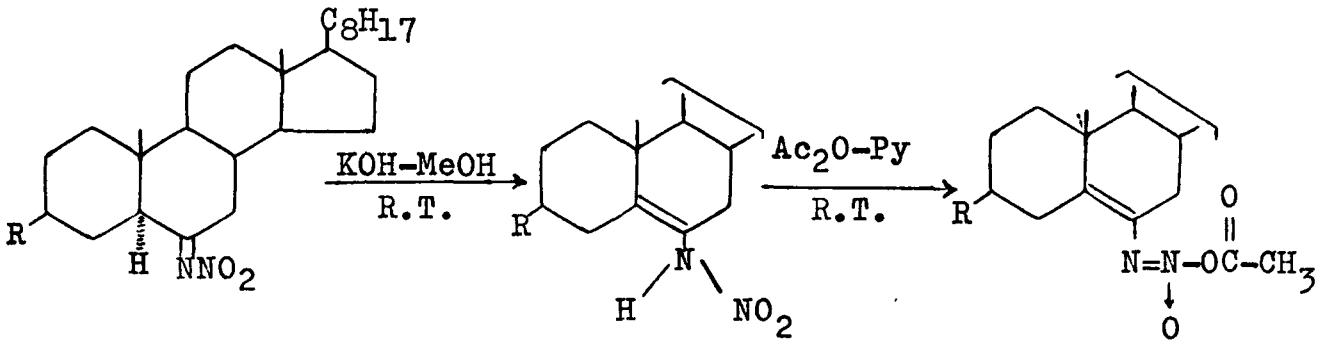
(XXX)

PART - TWO

Transformations of Steroidal Nitrimines

The nitrimines, obtained from the nitrosation reaction of ketoximes, undergo some interesting transformations to give a variety of products. We have therefore, carried out certain reactions of the steroidal nitrimines prepared by us. The transformations undertaken are, (i) isomerization by methanolic potassium hydroxide to give the nitroenamines, (ii) reduction with sodium borohydride in absolute ethanol to give nitroamines and (iii) thermolysis in refluxing xylene to give some interesting steroidal derivatives.

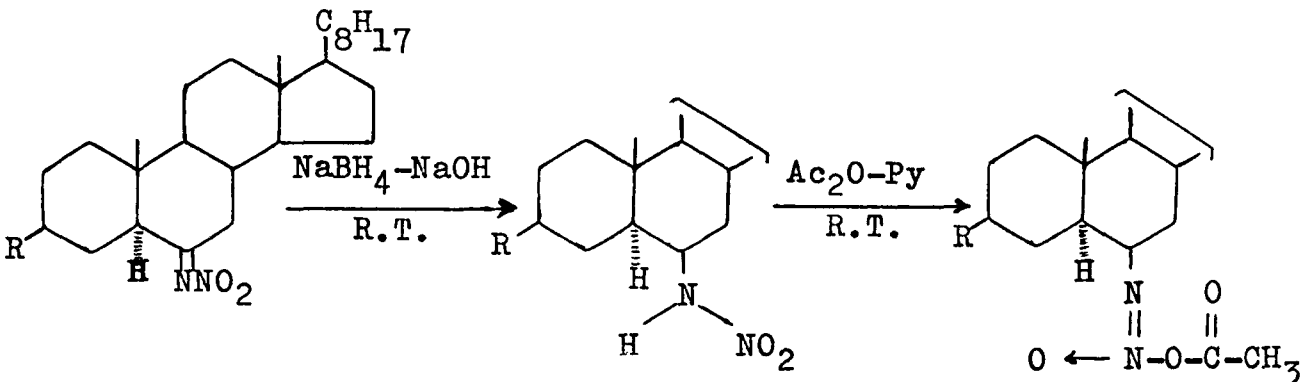
The isomerization of 6-nitrimino-5α-cholestane (X), 6-nitrimino-5α-cholestan-3β-yl chloride (XII) and 6-nitrimino-5α-cholestan-3β-yl acetate (XIV) with methanolic KOH at room temperature furnished their isomeric nitroenamines (XXXI-XXXIII) which were identified on the basis of their spectral properties. The reaction of these nitroenamines with acetic anhydride and pyridine gave their N-oxidoacetate derivatives (XXXIV-XXXVI).



(X)	R = H	(XXXI)	R = H	(XXXIV)	R = H
(XII)	R = Cl	(XXXII)	R = Cl	(XXXV)	R = Cl
(XIV)	R = OAc	(XXXIII)	R = OH	(XXXVI)	R = OH

The reduction of 6-nitrimino-5α-cholestane (X), 6-nitrimino-5α-cholestan-3β-yl chloride (XII), 6-nitrimino-5α-cholestan-3β-yl acetate (XIV) and 7-nitriminocholest-5-en-3β-yl chloride (XXIV) with sodium borohydride in absolute ethanol at room temperature gave their respective N-nitroamines (XXXVII-XL). These nitroamines were characterized on the basis of their spectral properties.

The acetylation of the nitroamines (XXXVII-XL) with acetic anhydride and pyridine at room temperature gave their respective O-acetyl-aci-nitroamines (XLI-XLIV).



(X) R = H

(XII) R = Cl

(XIV) R = OAc

(XXXVII) R = H

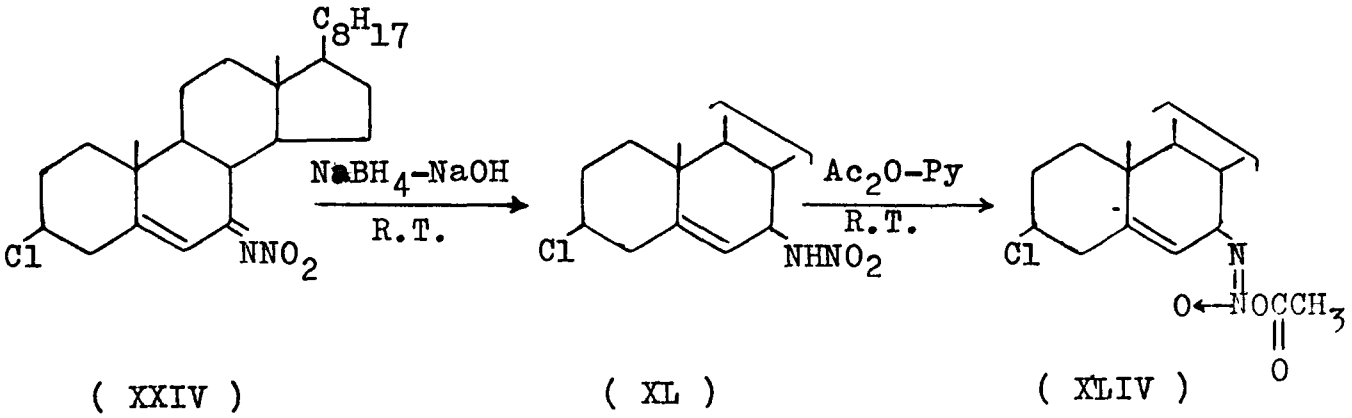
(XXXVIII) R = Cl

(XXXIX) R = OH

(XLI) R = H

(XLII) R = Cl

(XLIII) R = OH

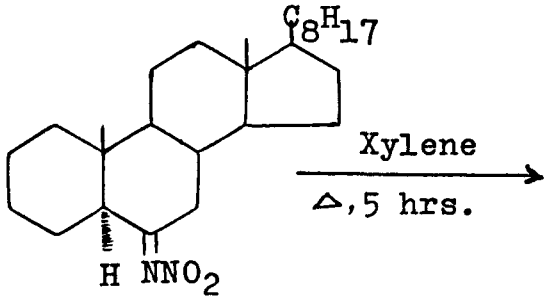


(XXIV)

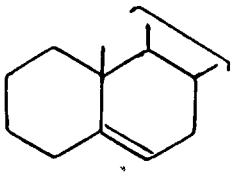
(XL)

(XLIV)

The thermolysis of 6-nitrimino-5α-cholestane (X), 6-nitrimino-5α-cholestan-3β-yl acetate (XII) and 7-nitriminocholest-5-en-3β-yl chloride (XXIV) in refluxing xylene resulted in the formation of some interesting steroidal derivatives. The products were identified on the basis of their spectral properties and comparison with authentic samples where available.

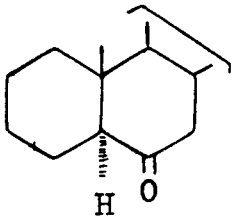


(X)

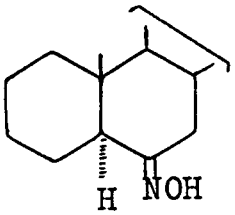


(XLV)

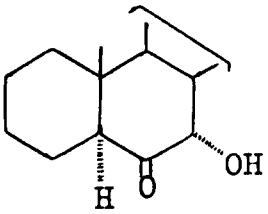
+



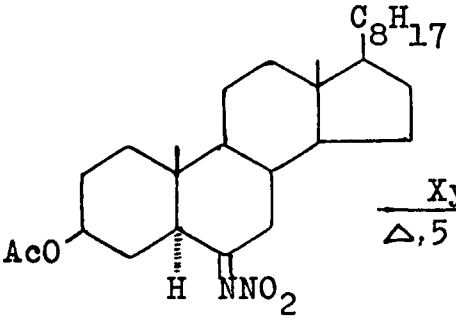
(XI)



(I)

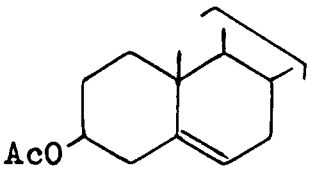


(XLVI)



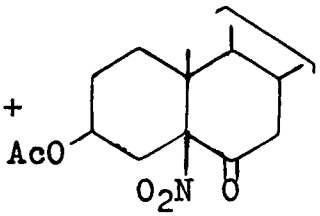
(XIV)

Xylene
△, 5 hrs.



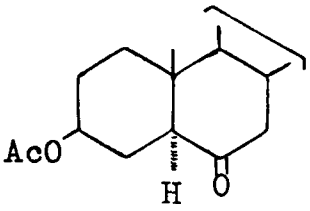
(XLVII)

+

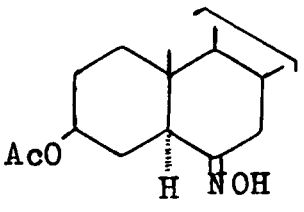


(XLVIII)

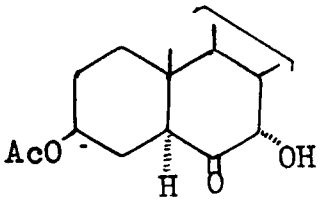
+



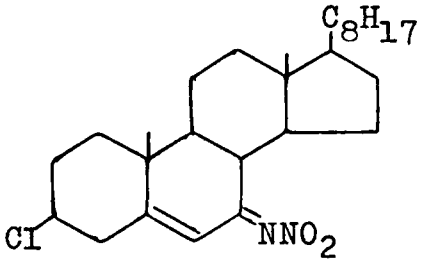
(XV)



(III)

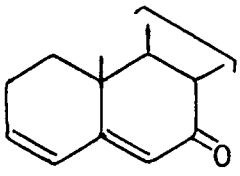


(XLIX)



(XXIV)

Xylene
△, 5 hrs.



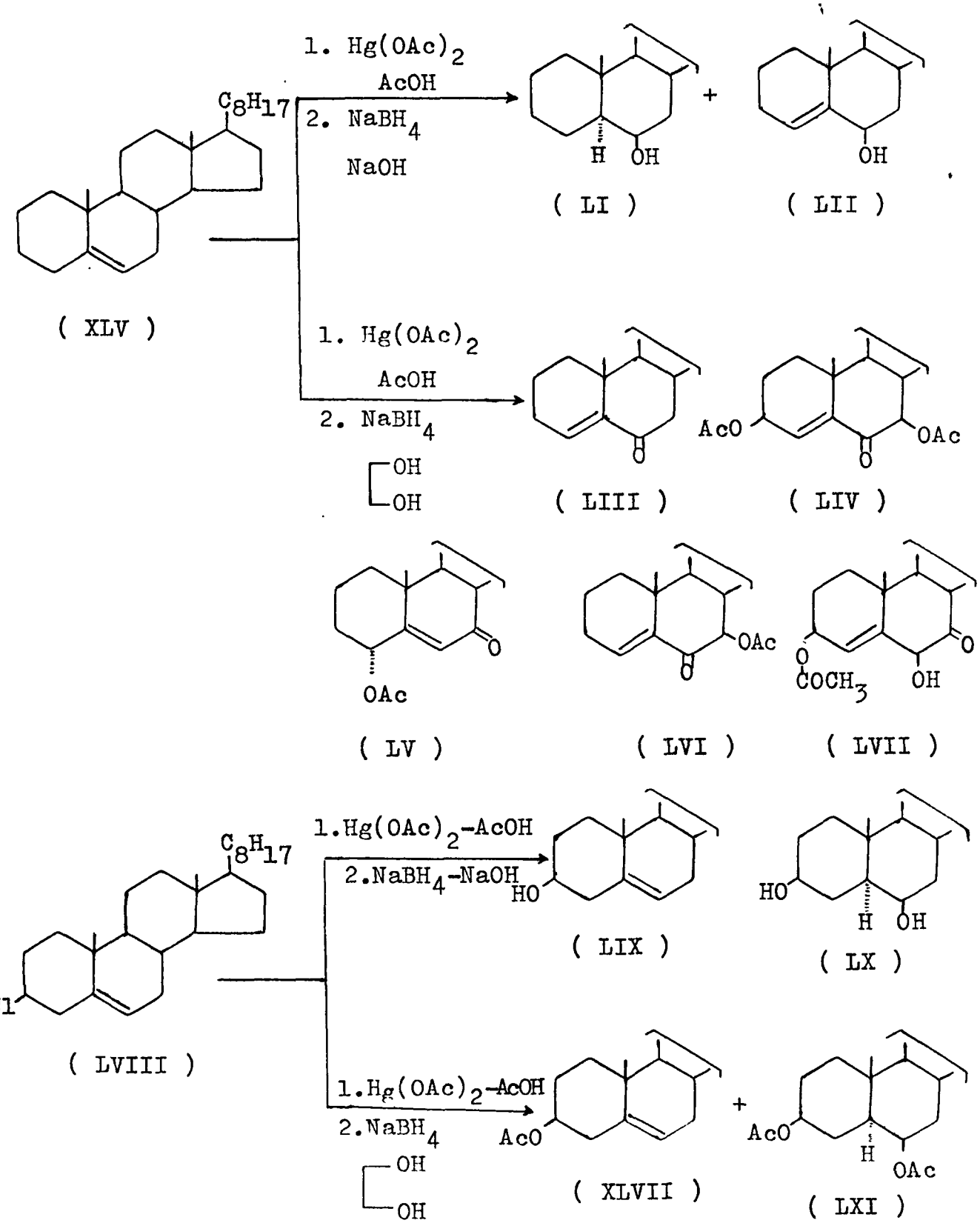
(L)

PART - THREE

A. Oxymercuration-Demercuration of Steroidal Olefins

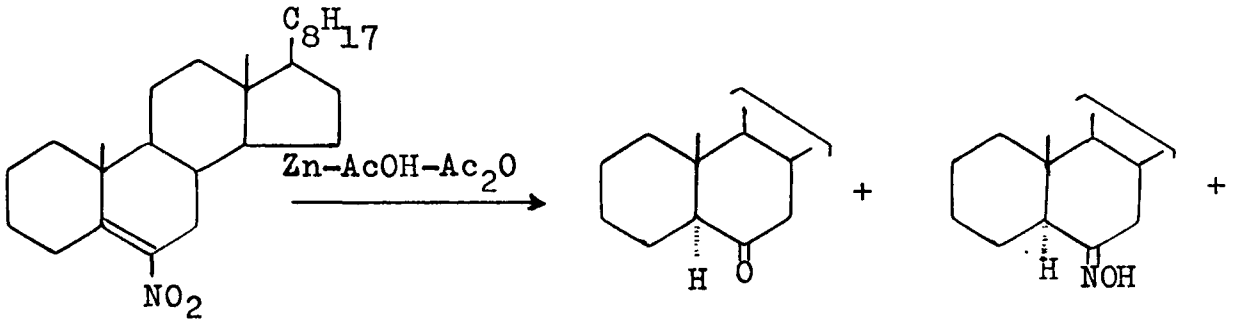
The oxymercuration-demercuration procedure provides a simple and convenient route to the Markownikoff hydration of carbon-carbon double bonds. The stereo- and regioselectivity attached with this reaction and the variations exhibited, particularly in the demercuration of the organomercurial adducts, prompted us to undertake the oxymercuration-demercuration of some of the easily accessible steroidal olefins in the cholestane series. The aim was to prepare some steroidal hydroxy ethers, previously prepared in our laboratory by mixed hydride reduction of cylic ketals, by empolying ethylene glycol and sodium borohydride at the demercuration step.

The oxymercuration of cholest-5-ene (XLV) and cholest-5-en-3β-yl chloride (LVIII) was done with mercuric acetate in acetic acid while the demercuration was affected under different reaction media. The products have been characterized on the basis of their spectral properties, chemical transformations and comparison with authentic samples where available. The results have been summarized in the following flowsheet.

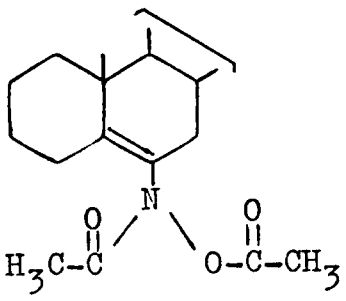

1. Hg(OAc)2
AcOH
2. NaBH4
NaOH
C8H17
(XLV)
(LI)
(LII)
1. Hg(OAc)2
AcOH
2. NaBH4
OH
OH
(LIII)
(LIV)
AcO
OAc
OAc
(LV)
OAc
(LVI)
O
COCH3
OH
(LVII)
1.Hg(OAc)2-AcOH
2.NaBH4-NaOH
C8H17
Cl
(LVIII)
HO
(LIX)
HO
H
OH
(LX)
1.Hg(OAc)2-AcOH
2.NaBH4
OH
OH
AcO
(XLVII)
AcO
H
OAc
(LXI)

B. Reduction of Steroidal Nitroolefins with Zn-AcOH Without Water

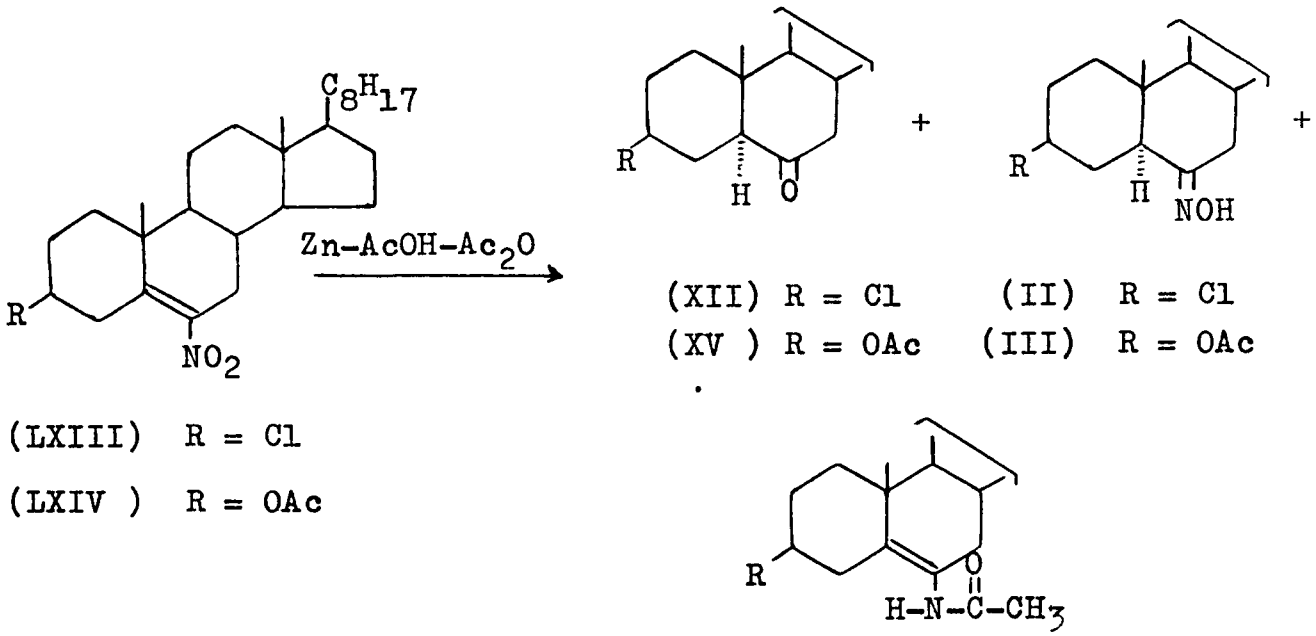
The conversion of nitroolefins into ketones by zinc-acetic acid-water reduction is a well known method. We made an attempt to carry out the reduction of steroidal nitroolefins, such as 6-nitrocholest-5-ene (LXII) and its 3β-chloro (LXIII) and 3β-acetoxy (LXIV) analogues, with zinc-acetic acid without added water in order to screen the intermediate involved in this reduction. We succeeded in isolating some acetylated enamine type of compounds, besides the respective ketones and oximes. The products obtained have been characterized on the basis of their spectral properties and comparison with authentic samples where available. The results have been summarized in the following flowsheet.



(LXII) (XI) (I)



(LXV)



(LXIII) R = Cl

(LXIV) R = OAc

(XII) R = Cl (II) R = Cl

(XV) R = OAc (III) R = OAc

(LXVI) R = Cl

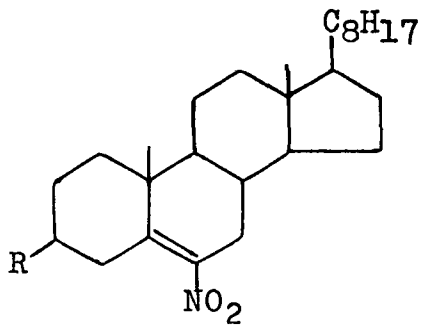
(LXVII) R = OAc

PART - FOUR

Mass Spectral Studies on Steroidal Nitro Compounds

During the last twenty five years or so the mass spectrometry has developed to become a very powerful analytical tool in the characterization of organic compounds. Virtually, every class of organic compounds had been subjected to this study and useful structure-spectra relationships have been established. It was, however, found that no significant studies have been made on the mass spectrometry of steroidal nitro compounds and this prompted us to undertake such studies on some of the

structurally related steroidal nitro compounds. These included the steroidal nitroolefins such as 6-nitrocholest-5-ene (LXII), 6-nitrocholest-5-en-3β-yl chloride (LXIII) and 6-nitrocholest-5-en-3β-yl acetate (LXIV).

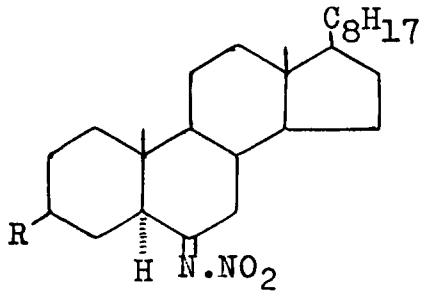


(LXII) R = H

(LXIII) R = Cl

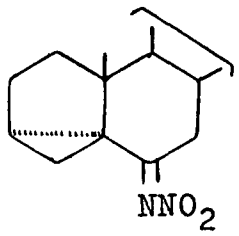
(LXIV) R = OAc

Besides these C-nitrosteroids, we also undertook the mass spectral studies on some N-nitrosteroids (nitrimines) which have been prepared in our laboratory. The nitrimines selected for the study were 6-nitrimino-5α-cholestane (X), 6-nitrimino-5α-cholestan-3β-yl acetate (XIV), 6-nitrimino-3α-5-cyclo-5α-cholestane (XVI), 7-nitriminocholest-5-ene (XXII), 7-nitrimino-cholest-5-en-3β-yl acetate (XXVI) and anti- and syn- forms of 3-nitriminocholest-4-ene (XVIII) and (XIX), respectively.

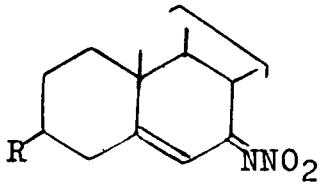


(X) R = H

(XIV) R = OAc

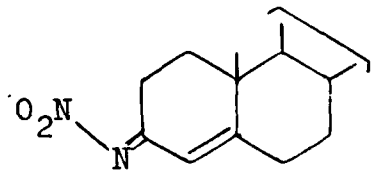


(XVI)

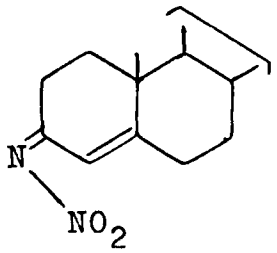


(XXII) R = H

(XXVI) R = OAc



(XVIII)



(XIX)

These studies were undertaken with a view to assess the effect of nitro group and to evaluate the effect of substitution on the fragmentation pattern. An attempt has also been made to visualize that how the fragmentation pattern of N-nitrosteroids differs from that of the C-nitrosterodis.

The proposed fragmentation pathways are supported in some cases by appropriate metastable peaks. The mechanisms suggested are only tentative in the absence of appropriate deuterated analogues and the accurate mass measurements.

INTRODUCTION

For the last fifty years, the chemistry of steroids has provided one of the most interesting and thoroughly explored areas for organic chemists. Though the discovery of cholesterol, the first steroidal compound to be known, was reported as early as 1812 by Cherveul, the dramatic expansion of steroidal chemistry came with the discovery of sex hormones in 1929-35. The physiological activity of steroidal hormones and their role in various metabolism, the discovery of several biologically active steroids, such as corticoids with their wide application in therapy and the preparation of modified steroids with interesting facets of chemistry, all afforded wealth of material of tremendous interest. Every year, a very large number of these compounds are screened for their chemical, biological, therapeutic and industrial potentials. The naturally occurring oxa-and aza-steroids, such as the steroidal alkaloids, have been found to be endowed with pronounced and specific biological activities.

The interesting physiological properties of the steroidal alkaloids and the discovery of a variety of oxygen and nitrogen containing heterocyclic compounds, with useful therapeutic properties, stimulated extensive research in oxygen and nitrogen

containing steroids and this resulted in the preparation of a variety of oxa-and aza-steroids with useful biological activities.

During the last decade the major effort of the chemists was directed towards modifications in the structure of steroids in order to enhance their valuable non-hormonal activity and increase selectively certain parameters of biological activity of the parent hormones. It also included the study of the activity-enhancing groups that would confer increased and oral activities. The broad spectrum of biological activities found in these compounds and the multiplicity of action displayed by certain individual members make them as one of the most intriguing class of compounds. The structural modification has not only furnished so many steroidal derivatives but has also led to the introduction of several less expensive, safer, more specific and potent therapeutic agents.

Our laboratory, concerned mainly with the synthesis of organic compounds and their identification and characterization by chemical and spectral studies, has been engaged for the last two decades in the preparation of modified steroids. The synthesis of a large number of oxa-and aza-steroids, mainly from cholestane and stigmastane series, has been reported. Beckmann rearrangement, Schmidt reaction and Baeyer-Villiger oxidation have been extensively used for these syntheses. The characterization of these compounds has been achieved by chemical and spectral methods,

employing UV, IR, NMR spectroscopy and Mass spectrometry.

In the present work an attempt has been made to use a less familiar but interesting nitrosation reation of steroidal ketoximes to obtain steroidal nitrimines. These steroidal derivatives have been subjected to some interesting transformations resulting in the formation of modified steroidal compounds. These have been identified by spectral and chemical methods. In some cases abnormal products have been obtained and this has offered scope for some mechanistic and stereochemical studies also.

We have also carried out the oxymercuration-demercuration reaction of steroidal olefins in an attempt to prepare steroidal hydroxyethers, which have previously been obtained by the mixed hydride reduction of the cyclic ketals.

The mass spectral studies of related C-nitro and N-nitro compounds have been undertaken in order to establish structure-spectra relationship.

T H E O R E T I C A L

PART - ONE

NITROSATION REACTION

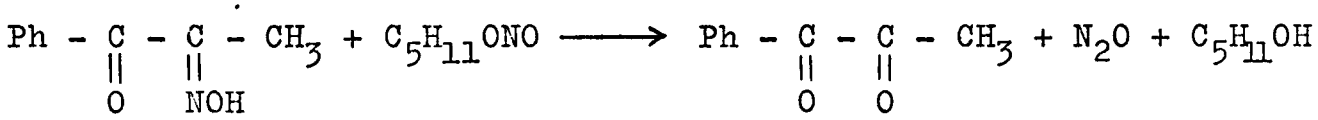
The nitrosation reaction consists in the replacement of an activated α-hydrogen by a nitroso group or its equivalent with the formation of a nitroso derivative. This reaction was discovered by Meyer in 1873 when he found that careful acidification of an alkaline solution of a nitroparaffin and an alkali nitrite converts a primary nitroparaffin into a nitrolic acid[1] and a secondary nitroparaffin into a pseudonitrole[2,3]. Approximately at the same time Tilden established that a nitroso group can be introduced into an organic structure through the addition of a nitrosating agent across a carbon-carbon double bond[4].

Nitrosation reactions have been carried out by nitrous acid, nitrosyl chloride, nitrosyl sulphuric acid, nitrous fumes and esters of nitrous acid. An acid or a base is usually added as catalyst with the last two reagents.

Oximes react with nitrosating agents in a wide variety of ways depending upon the structure of the oxime, the nature of the nitrosating agent and the conditions of the reaction. Some of these reactions have been of considerable synthetic utility for many years. Oximes contain three sites which are potentially reactive, but in their reaction with nitrosating

agents (in which the attacking species presumably is either the nitrosyl cation, $\overset{+}{N}O$ or nitrogen dioxide radical, $\dot{N}O_2$), attack occurs predominantly at carbon or nitrogen.

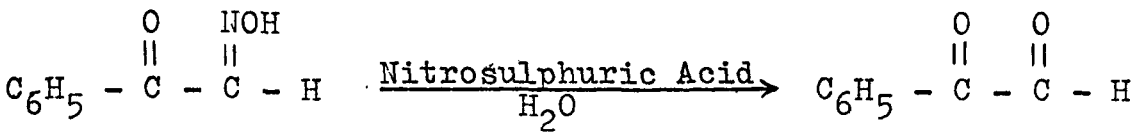
The reaction of oximes with nitrosating agents to regenerate the parent carbonyl compound is in fact well known and has been observed in the absence of donor solvents such as water, alcohol, etc. The nitrosative deoximation was first observed by Claisen and Manasse[5] who treated α-oximinopropiophenone (I) with amyl nitrite to produce the corresponding diketone (II) and nitrous oxide.



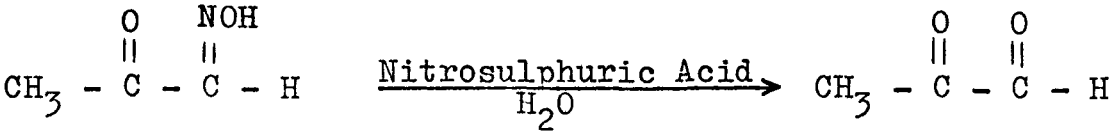
(I) (II)

Since its discovery, the nitrosative deoximation reaction has extensively been used as a synthetic tool for the conversion of oximes to ketones[6].

Neuberg, et al.[7-9] successfully deoximated phenylglyoxal aldomixe (III) to phenylglyoxal (IV) by the aqueous nitrosulphuric acid and by oxides of nitrogen in aqueous medium. Neuberg and Hofmann[7,8] have also deoximated pyruvaldoxime (V) to pyruvaldehyde (VI) by this method and reported the formation of nitrous oxide as by product.



(III) (IV)

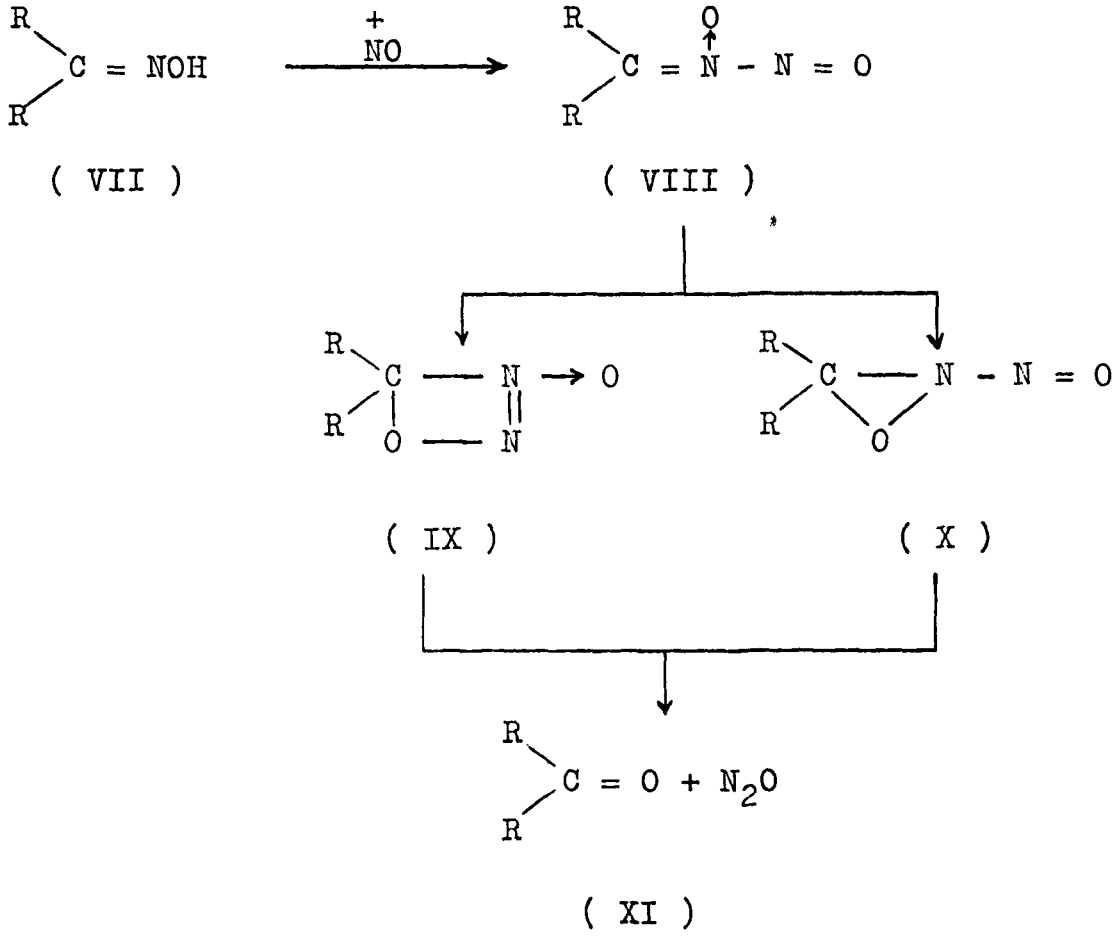


(V) (VI)

The importance of nitrosative deoximation increased further with the invention of Barton's nitrite photolytic reactions[10], utilized in forming oximes directly from hydrocarbons.

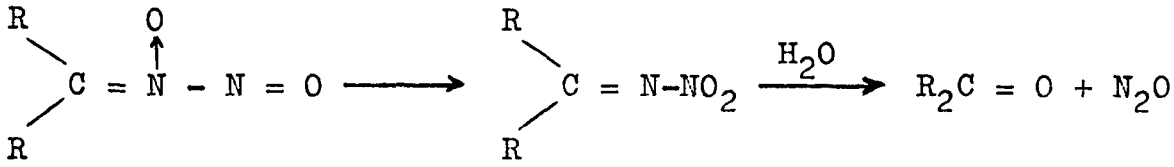
The mechanism of deoximation and the nature of the intermediates formed are only partly understood. The frequent formation of nitrous oxide as a by product of nitrosative deoximation suggests the occurrence of an initial attack of a nitrosating entity, such as nitrosonium ion, upon the nitrogen of the oxime (VII) to give an intermediate (VIII). This intermediate then rearranges intramolecularly either through the formation of a four—membered ring (IX) or a three-membered ring (X). The former process is analogous to that proposed for the intramolecular decomposition of nitrosimines to ketones and nitrogen[11]. These cyclic intermediates finally lose a molecule of nitrous oxide and regenerate the ketone (XI) as shown in Scheme 1.

Scheme 1



This mechanism is further suggested by many instances[12-16] in which the pernitroso derivatives, prepared by the treatment of oximes with nitrosating agents, were decomposed readily to give nitrous oxide and the corresponding ketones. Alternatively, it has also been suggested that the intermediate (VIII), formed by the N-nitrosation of oximes, rearranges to a nitrimine structure (XII) which undergoes subsequent hydrolysis to

regenerate the corresponding ketone (XI).



(VIII) (XII) (XI)

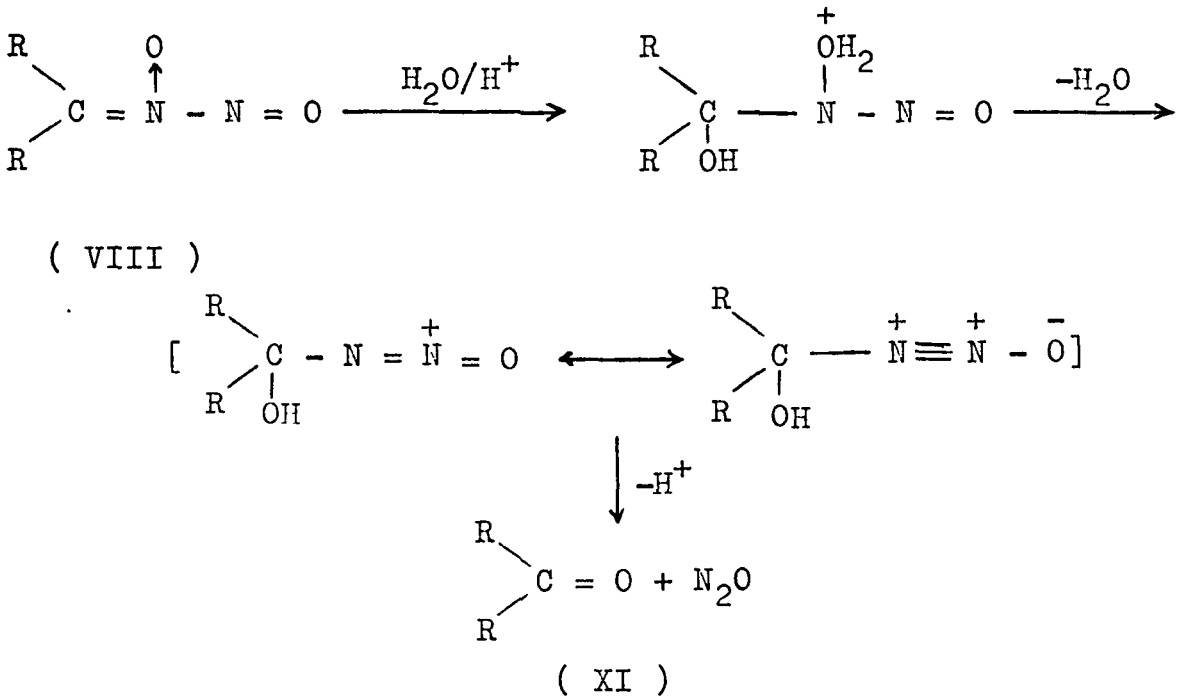
There have been occasional reports[12-14] of the formation of nitrogen rather than nitrous oxide in the nitrosative deoximation. The intermediate formation of an unstable diazo nitrate appears to be involved in such cases[11-13,17].

Wieland and Grimm[18] made an attempt to settle the correct mechanism by tagging the nitroso oxygen with ^{18}O and they determined that approximately 90% of the label appeared in nitrous oxide. This experiment rules out the intermediates (IX) and (XII) as these will give 0% ^{18}O and 50% ^{18}O in N_2O, respectively, and as a result these authors claimed that intermediate (X) must be involved. This suggestion was however, not acceptable due to two observed facts. Firstly, many oximes, particularly those in which the oxime double bond is sterically hindered, do not undergo deoximation under the conditions but rather are converted to nitrimine (XII). It is not clear how the bulky group would favour oxygen migration over ring closure. On the basis of Thorpe-Ingold effect[19], one might have anticipated

such oximes to deoximate even more readily if small ring formation were a critical step. Secondly, it is known that semicarbazones are converted to ketones by nitrous acid[20]. Since there is no oxygen atom in these derivatives similar to that necessary to form an intermediate such as (X), there must exist another route to obtain the ketone from N-nitroso intermediate (VIII).

Freeman[21a] suggested a mechanism for the nitrosative deoximation which involves the hydrolysis of the intermediate (VIII). This mechanism accounts for all the observed facts. The crucial point in this mechanism is to avoid any intermediate in which the N-oxygen atoms lose their identity. The reaction might occur as shown in scheme 2.

Scheme 2

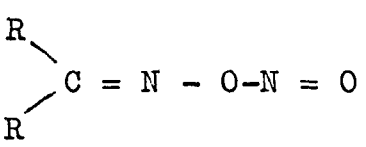


The important step in this mechanism is the facile loss of the hydroxyl group followed by nitrous oxide from the nitrosohydroxylamine intermediate rather than the loss of hydroxylamine in which the oxygen would be scrambled.

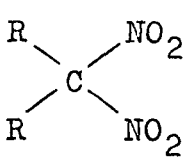
Recently, a very similar mechanism based on ^{15}N tracer studies has been proposed[21b]. The work actually bears more on the origin of nitrogen and nitrous oxide from deoximation reaction, since all mechanisms proposed show one nitrogen in the nitrous oxide coming from oxime and one from nitrous acid.

In addition to the deoximation reaction, a number of oximes, particularly those in which the oxime double bond is sterically hindered, react with nitrous acid and other nitrosating agents to produce pernitroso compounds[22]. All of these oximes are characterized by the presence of a quaternary carbon adjacent to the oxime function.

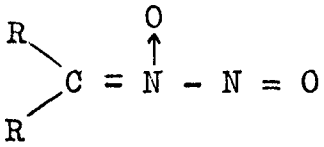
A number of structural formulae have been suggested for these pernitroso compounds. Angeli and his coworkers[23] considered these derivatives to have structures, such as (XIII) or (XIV). The oxime nitrite structure (XIII) and the gem dinitro structure (XIV) were discarded in favour of the N-nitrosoxime structure (VIII)[24]. This later formulation was favoured by Fusco and his coworkers[25] for pernitrosomesityl oxide, which was, however, subsequently proved to be incorrect[26].



(XIII)

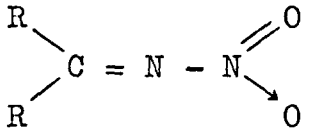


(XIV)

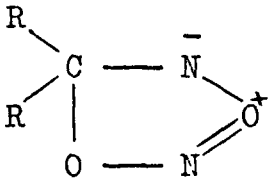


(VIII)

Scholl[27], however, abandoned all these structures and suggested a nitrimine structure (XII) on the basis of his preparation of an analogous compound from pinacolone. The nitrimine structure was also favoured by Wright, et al.[28] because of the similarity in chemical behaviour of pernitrosocamphor and furfural nitrimine. Recently, a mesoionic structure (XV) has also been suggested[29].

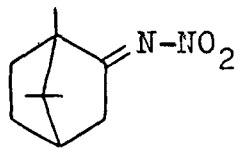


(XII)

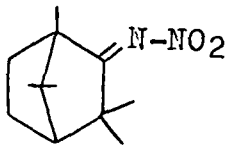


(XV)

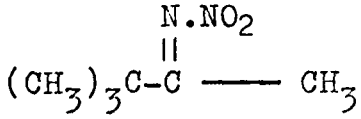
Preliminary evidence was reported to support the nitrimine structure for pernitrosocamphor (XVI)[30]. Additional evidence for such type of structure came from pernitrosofenchone (XVII) and pernitrosopinacolone (XVIII)[22].



(XVI)



(XVII)



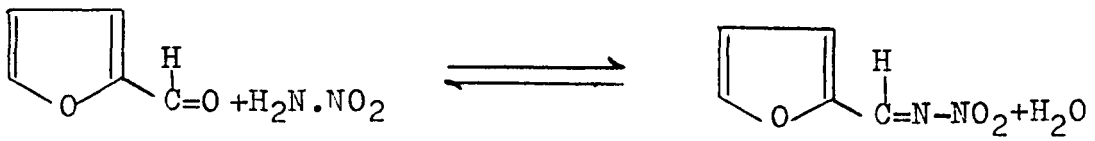
(XVIII)

The infrared spectrum of each of these compounds contains strong bands at 1560-1570 and 1310-1320 cm^{-1} and a medium band at 1620-1640 cm^{-1}. The two strong bands may be assigned to the asymmetric and symmetric stretching vibrations of the nitro group[31] and the medium band to the imine (C=N) stretching frequency[31] of the nitrimine structure.

The oxime nitrite structure (XIII) can not be accounted for by these spectra as nitrites exhibit a characteristic doublet[32] in the region 1650 and 1620 cm^{-1}. The spectral characteristics of structures (XIV) and (VIII) are only speculative but it is difficult to assign these three bands to specific vibrations associated with these structures. For instance, nitrosoamines do not absorb above 1500 cm^{-1}, whereas nitrones usually have one intense band in the 1750-1620 cm^{-1} region[33].

The ultraviolet spectra of compounds (XVI), (XVII) and (XVIII) are characterized by low intensity absorption ($\varepsilon_{max.}$ 500-600) at 270 nm. This wavelength must be associated with the pernitroso function, but the nature of the transition is unknown. The spectra are not compatible with those of nitrosoamines[34], nitrones[33] or nitrites[34], ruling out structures (XIII) and (VIII). The mesoionic structure (XV) would be expected to lead to a high intensity band[35].

In view of the differences in opinion regarding the structure of the pernitroso derivatives, Wright, et al.[28] thought it worthwhile to prepare a nitrimine of reliable structure. They succeeded in preparing the furfuralnitrimine (XX) by the simple condensation of furfural (XIX) with nitramide without catalyst or solvent. The nitramide probably reacted as such because it could not be replaced by hyponitrous acid, a possible contaminant.

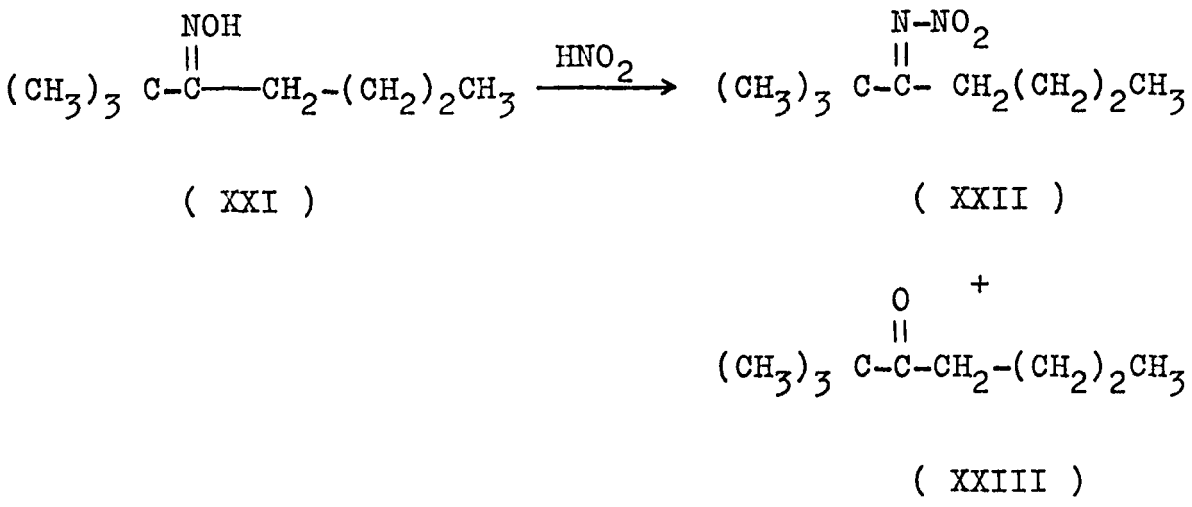


(XIX) (XX)

Nitrimines have also been reported to be formed by the action of nitrosyl fluoride on steroid-4- and 5-enes[36]. In this reaction the intermediate olefin adduct, the fluoronitroso compound tautomerizes to fluoroxime which is further nitrosated to yield the fluoronitrimine. In these cases one of the position on adjacent quaternary carbon is occupied by a fluorine atom.

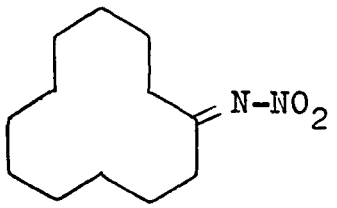
Houben and Pfankuch[37] have devised a very simple method for bringing about the nitrosation reaction of ketoximes. They prepared 3-nitrimino-2,2-dimethylheptane (XXII) by the action of nitrous acid on 3-oximino-2,2-dimethylheptane (XXI). The

reaction was performed at room temperature and resulted in 66% yield of the nitrimine along with a small amount of the parent ketone, 3-oxo-2,2-dimethylheptane (XXIII).

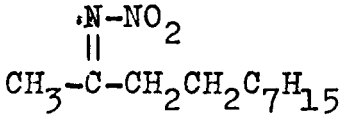


(XXI) (XXII) (XXIII)

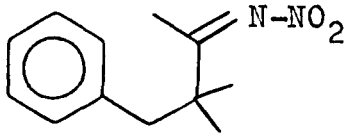
This method was later used by Buchi and Wuest[38] for the preparation of nitrimines (XXIV), (XXV), (XXVI), (XXVII) and (XXVIII) from their respective oximes.



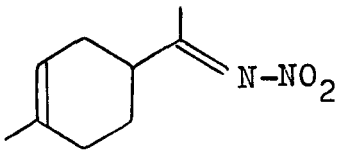
(XXIV)



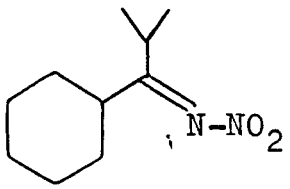
(XXV)



(XXVI)

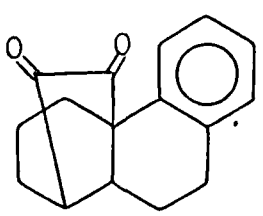


(XXVII)

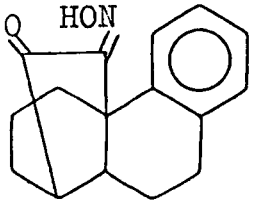


(XXVIII)

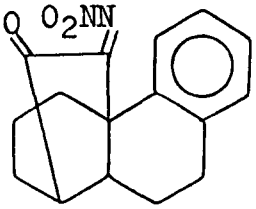
α-Oximinoketones also give rise to nitrimines when subjected to nitrosation reaction. There is at least one example of α-ketonitrimine (XXXI) prepared by the action of a nitrite ester on a diketone (XXIX) in the presence of excess base, a reaction in which the derived α-oximinoketone (XXX) undergoes further nitrosation[39].



(XXIX)

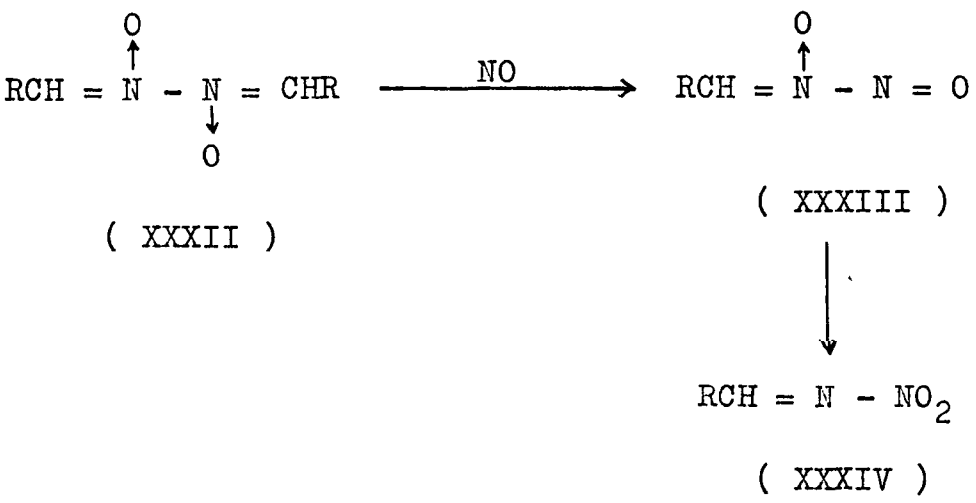


(XXX)



(XXXI)

Nitrimines have also been reported by the reaction of azine bis (oxide) (XXXII) with nitric oxide[40]. While the reaction appears at first glance to be a free radical reaction, little is known about the true mechanism. Presumably an N-nitrosonitrone (XXXIII) is the first formed intermediate which rearranges to nitrimine (XXXIV).

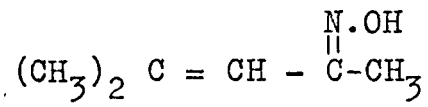


The structure of the compound derived from azine bis (oxide) was a controversial matter for a long time but appears finally to have been settled as involving a nitrimino group. The assignment is based on their spectral properties and facile reduction to nitramines. The hydrolysis of these compounds to ketones and nitrous oxide, the known decomposition products of nitramide is also consistent with this formulation, as is the formation of furfural nitrimine from the reaction of furfural with nitramide[26].

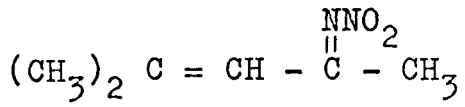
There exists a close relationship between deoximation and the formation of nitrimines. It seems reasonable to assume that the first step in both the cases is the formation of a nitrogen-nitrogen bond by nitrosation of the oxime nitrogen. The fact that the oximes that are converted to nitrimines contain a quaternary carbon adjacent to the C-N double bond suggests that the attack of water at that bond is hindered in those compounds allowing the nitrosonitrone function to survive and ultimately to rearrange (possibly by intramolecular disproportionation) to nitrimine which can in turn be hydrolyzed under more forcing conditions[41]. A particularly striking example of the effect of steric hinderance on nitrimine stability has been reported by Barton, et al.[42]. However, easily hydrolyzed nitrimines have been isolated when nonhydrolytic reactions or conditions were employed[36,40].

α,β-Unsaturated ketoximes are converted to a series of novel heterocycles upon treatment with nitrosating agents.

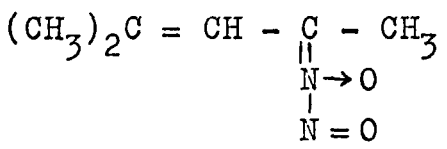
These compounds were discovered when it was realized that the nitrosation of mesityl oxide oxime (XXXV) with nitrite ester in acetic acid did not yield the ordinary nitrimine[43] (XXXVI) as suggested by Scholl[27] on the basis of his investigations on pernitroso compounds of terpene series. The nitrimine structure was first rejected by Fusco[25] who subsequently proposed a structure containing the N-nitrosonitrone function (XXXVII). Later investigators could not confirm or deny either structure but believed that pernitrosomesityl oxide has a different structure than did pernitrosocamphor (XVI) due to the differences in their physical and chemical properties. The spectral analysis of these compounds confirmed that they are different from other pernitroso compounds and the structure (XXXVIII) was assigned to the pernitrosomesityl oxide.



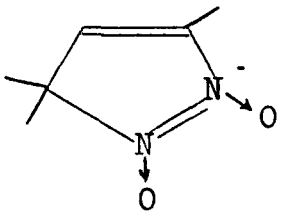
(XXXV)



(XXXVI)



(XXXVII)

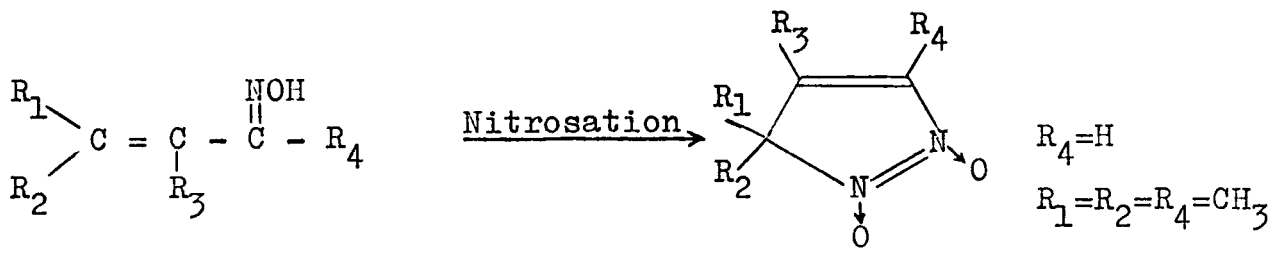


(XXXVIII)

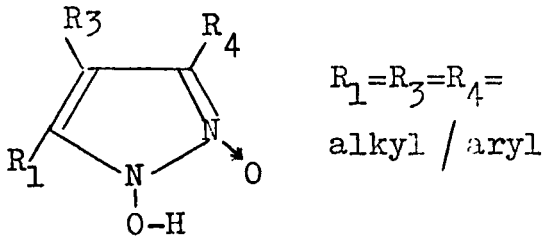
The IR spectrum of the pernitrosomesityl oxide shows no absorption due to an N-nitro group in the region of 1500-1600 cm^{-1} (asymmetric stretching) or 1250-1350 cm^{-1} (symmetric stretching). The strong band at 1485 cm^{-1} is however most probably associated with N=N→O function. The UV spectrum of the compound ($\lambda_{max.}$ 310 nm, $\varepsilon_{max.}$ 4500; $\lambda_{max.}$ 216 nm, $\varepsilon_{max.}$ 9740) also indicates that a nitrimine function is not present and suggests a highly conjugated system. The NMR spectrum of the pernitrosomesityl oxide furnishes critical evidence concerning its structure. The spectrum was quite different from that of the mesityl oxide oxime itself, indicating the presence of a vinylic proton, a methyl group attached to an unsaturated centre and two methyl groups attached to a saturated carbon atom. The splitting of the signal due to the single methyl group is of such an order as to suggest its coupling with the vinylic proton through a double bond. On the basis of these spectral data it was possible to suggest that these compounds are pyrazolenine dioxide derivatives and the pernitrosomesityl oxide was given the structure (XXXVIII).

Examination of the literature revealed that other α,β-unsaturated ketoximes had yielded nitrosation products of uncertain structure. It has however, been established that all of these are related to the mesityl oxide product with further elaboration of independent molecules, dependent upon structures. The results may be summerized as shown in scheme 3.

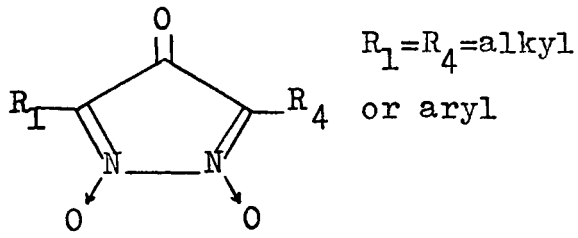
Scheme 3



(XXXVIII)



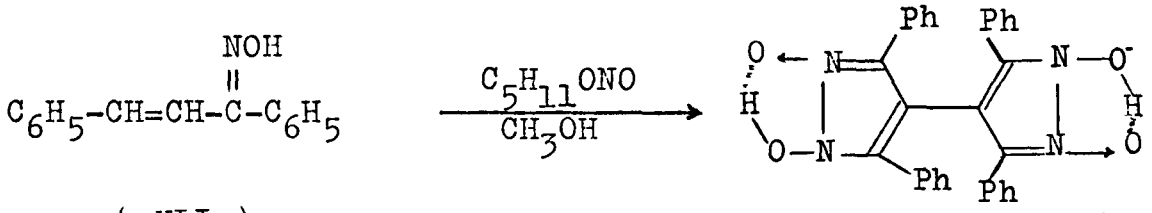
(XXXIX)



(XL)

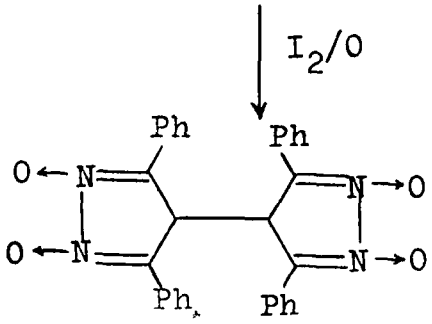
The compounds of the type (XXXIX), N-hydroxy-N'-oxide, are tautomers of the mesityl oxide type product (XXXVIII). These unique compounds are relatively strong organic acids, form complexes with metal ions and undergo electrophilic substitution reaction at 4-position of the pyrazole ring[44].

A compound of structure (XXXIX) has, however, been never isolated from these reactions. In an attempt to obtain such a compound the nitrosation of benzalacetophenone oxime (XLI) was carried out using isoamyl nitrite in a neutral medium[45]. From this reaction, a white solid with properties similar to those of N-hydroxy-N'-oxide was isolated in 50% yield. However, the structure of this compound was shown not to be like (XXXIX) but rather a dimeric structure (XLII). The compound (XLII) was readily oxidized by a variety of oxidizing agents, but most conveniently with iodine to a shining reddish solid with assigned structure (XLIII). This compound can not be a planar molecule because of the interference of the four ortho phenyl groups. Some preliminary ESR experiments suggest possible biradical character for this compound, but details about its structure await further investigations.



(XLI)

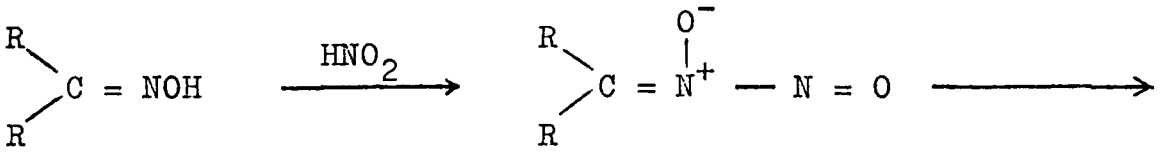
(XLII)



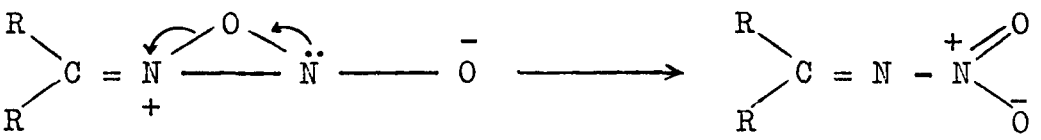
(XLIII)

Several attempts have been made to explain the mechanistic pathways involved in nitrimine formation and the formation of pyrazolenine dioxide derivatives. The major barrier in explaining the nitrimine formation has been in rationalizing the formation of a nitro group from the reactants. The first step in both the saturated as well as α,β-unsaturated ketoximes is most probably the N-nitrosation to give a nitrosonitrone intermediate. This intermediate may be considered to be similar to a disulphoxide which apparently disproportionates intramolecularly to form a thiol sulphonate[46]. (Recent investigations, however, cast some doubt on the universality of this mechanism[47]). The nitrosonitrone intermediate then undergoes oxygen transfer through a three membered ring which is probably favoured by the relief of steric strain and by the highly electrophilic nature of the nitroso group. (Scheme 4).

Scheme 4



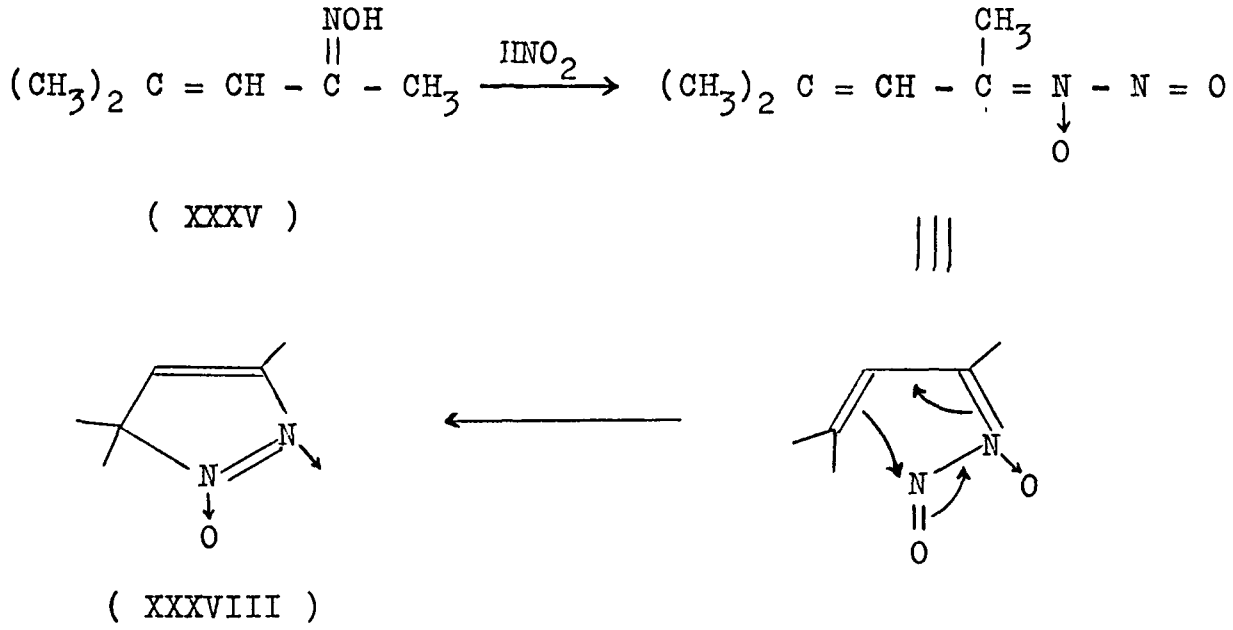
(VII)



(XII)

In the case of pernitrosomesityl oxide, electrons are available from the double bond, and the ring closure rather than oxygen migration occurs to give pyrazolenine dioxide derivative (Scheme 5).

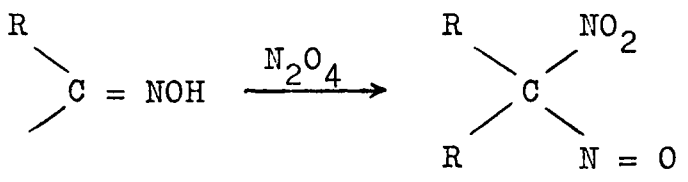
Scheme 5



(XXXV)

(XXXVIII)

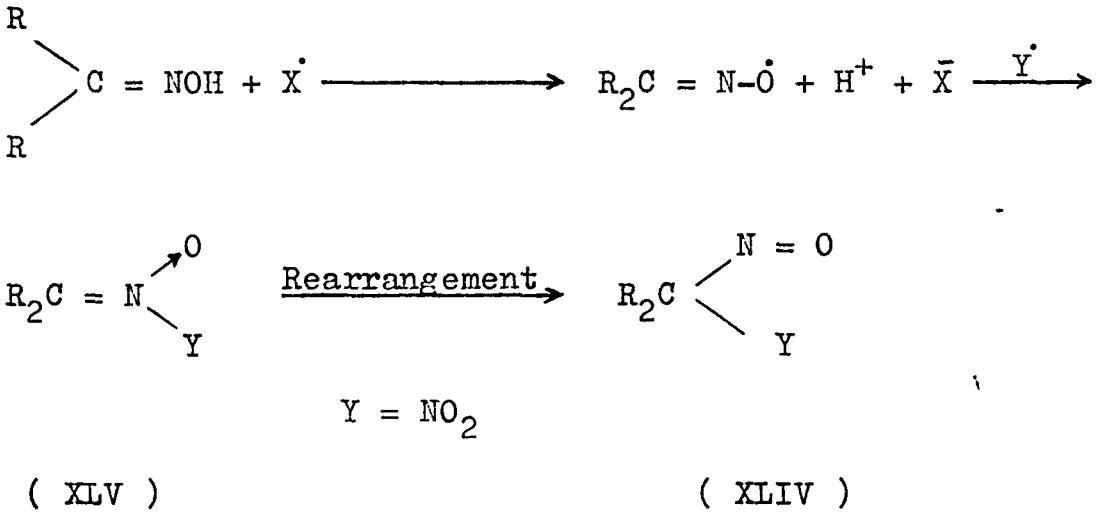
Many aliphatic ketoximes, when subjected to nitrosation reaction with dinitrogen tetroxide in ether, form gem nitronitroso compounds commonly called pseudonitroles (XLIV)



(XLIV)

Riebsomer[48] has reviewed the early literature of this reaction. Though this reaction is not of much synthetic value, its mechanism may be of some interest. A number of mechanisms have been postulated but the most reasonable one[49] involves a one electron transfer from the oxime to an electrophilic radical, coupling of the iminoxy radical[50] with any available radical and finally rearrangement to the observed product (XLIV) (Scheme 6).

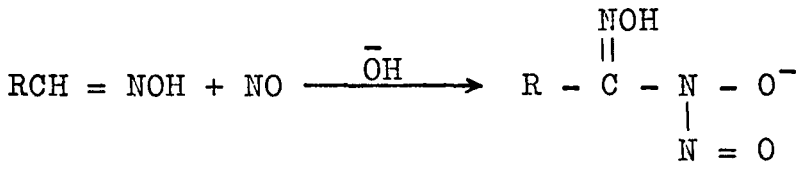
Scheme 6



(XLV) (XLIV)

Some support for this mechanism has been found in the fact that acylation of nitronate anion leads to ketone by way of α-acetoxynitro compound[51], indicating that an intermediate (XLV) does in fact rearrange to a nitroso compound. This mechanism suggests a common intermediate for the nitrosation of nitronate

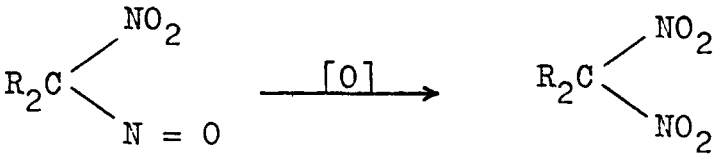
anion and the reaction of oximes with nitrogen tetroxide, the reactions which lead to α-nitronitroso compounds. It also suggests that the radicals which are not easily reduced to stable anions will not react in the same way. In fact nitric oxide reacts with oxime (XLVI) like an acylating agent to produce eventually nitrohydroxylamine derivative (XLVII)[52].



(XLVI) (XLVII)

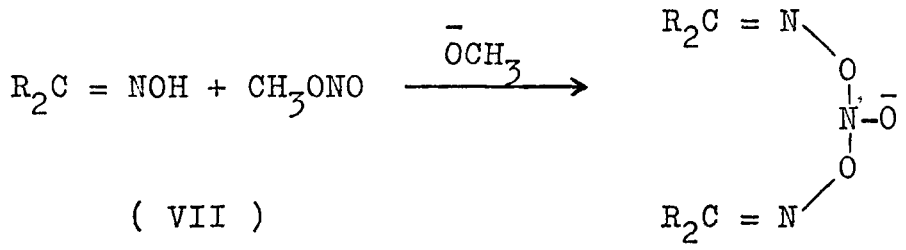
However, if an iminoxy radical is generated in the presence of nitric oxide, coupling occurs at nitrogen to yield the nitrimines[53].

In certain cases the pseudonitrole formed as a result of nitrosation undergoes oxidation to give gem-dinitroalkane (XIV)[54]. Although, this reaction is of limited scope, it provides one of the few routes to gem-dinitroalkanes.



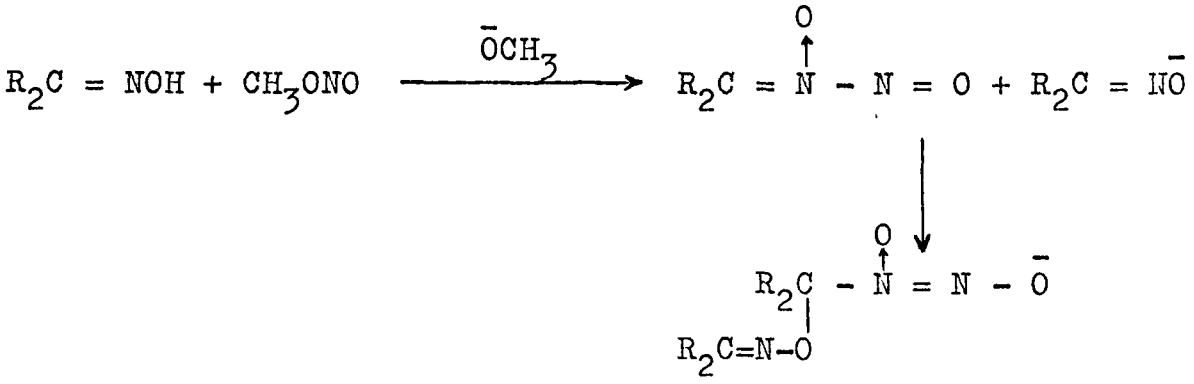
(XLIV) (XIV)

Forster, et al.[55] proposed that treatment of ketoximes with methyl nitrite in the presence of methoxide ion produced a novel O-nitrosation product (XLVIII).



(VII) (XLVIII)

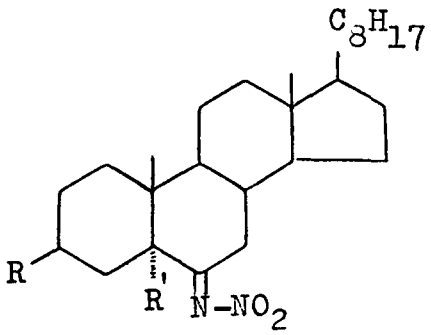
The structure of the compound (XLVIII) was certainly not established unequivocally, and an alternate structure more analogous to that from other reactions of this type would be (XLIX), formed possibly as shown below.



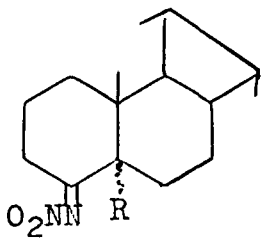
(XLIX)

The products of hydrolysis of this compound, ketone, oxime and nitrous oxide are in fact better rationalized in terms of structure (XLIX) than they are with the Forster structure (XLVIII).

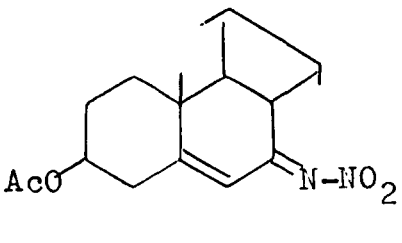
Recently, Suarez, et al.[56] have reported certain steroidal nitrimines in an attempt to prepare steroidal N-nitroamines. They treated some cholest-4-, and 5-enes with sodium nitrite and formic acid in the presence of BF_3-etherate and obtained 6-nitrimino-5α-cholestane-3β, 5-diol diformate (L), 6-nitrimino-5α-cholestan-5-yl formate (LI), 4-nitrimino-5α-cholestan-5-yl formate (LII) and 4-nitrimino-5β-cholestan-5-yl formate (LIII). They also prepared 6-nitrimino-5α-cholestan-3β-yl acetate (LIV) and 7-nitriminocholest-5-en-3β-yl acetate (LV) by carrying out the nitrosation of their respective oximes with sodium nitrite and acetic acid.



	R	R'
(L)	HCO_2	HCO_2
(LI)	H	HCO_2
(LIV)	OAc	H

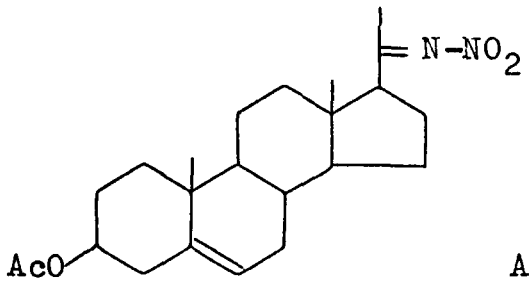


(LII) R = α-H
(LIII) R = β-H

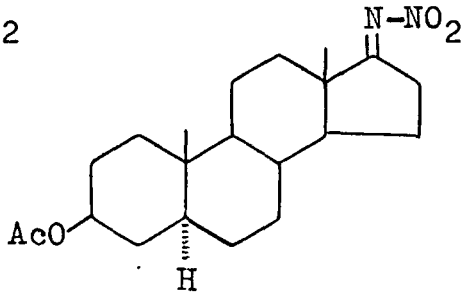


(LV)

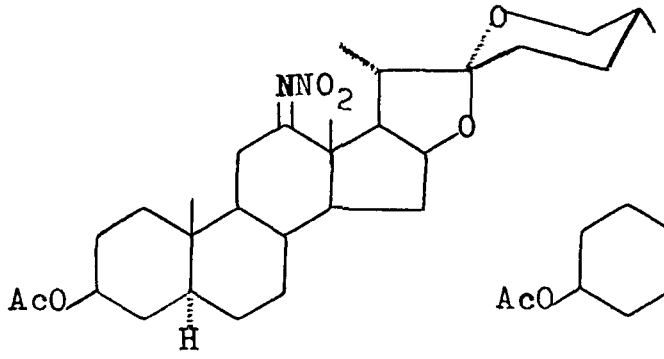
Suarez, et al.[57] have also prepared 20-nitriminopregn-5-en-3β-yl acetate (LVI), 17-nitrimino-5α-androstan-3β-yl acetate (LVII), 12-nitrimino-(25R)-5α-spirostan-3β-yl acetate (LVIII) and 23-nitrimino-(20S, 22S, 25S)-5β-spirostan-3β-yl acetate (LIX) by the nitrosation reaction of their respective oximes.



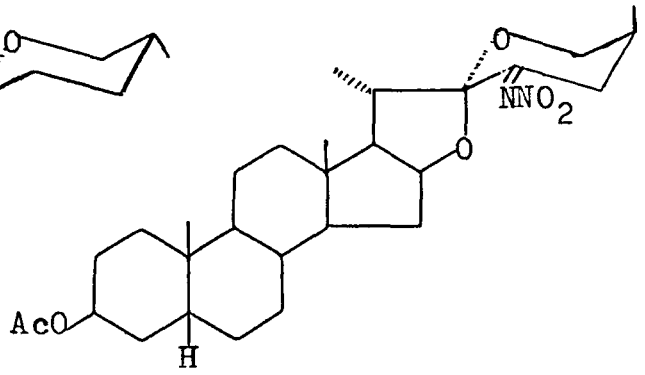
(LVI)



(LVII)



(LVIII)



(LIX)

PART - TWO

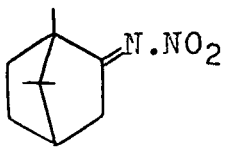
TRANSFORMATIONS OF NITRIMINES

The nitrimines, prepared by the action of nitrosating agents on ketoximes, undergo a variety of transformations furnishing compounds of synthetic interest. The important transformations which the nitrimines undergo are as follows:

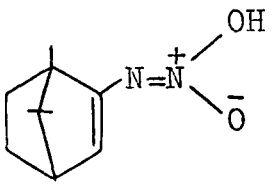
1. Salt Formation/Isomerization.
2. Reduction.
3. Transformation to Acetylenes and Allenes.
4. Photochemical and Thermolytic Transformations.

1. Salt Formation/Isomerization

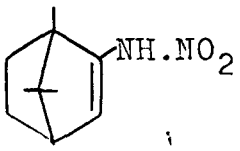
Nitrimines with neighbouring methine and methylene groups form salts on treatment with alcoholic alkali[58]. Acidification of the salt derived from pernitrosocamphor (XVI), for example, gave a crystalline tautomer, isopernitrosocamphor which on storage slowly returned back to the more stable pernitrosocamphor[59]. The stable modification was given the name nitrimine while the unstable form was assumed to be the nitronic acid (LX) rather than the N-nitroenamine (LXI).



(XVI)

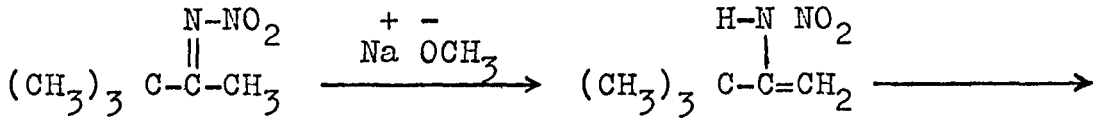


(LX)

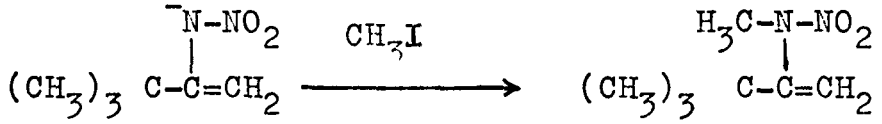


(LXI)

In his original investigations on pernitrosopinacolone (XVIII), Scholl[27] reported that it was converted to a salt by sodium methoxide and that this salt was methylated by methyl iodide to the vinyl nitramine (LXII).



(XVIII)

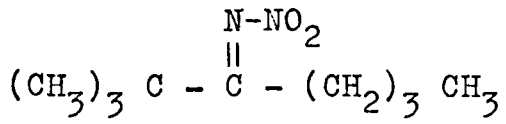


(LXII)

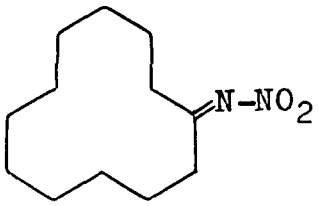
Since this transformation bears directly on the structure of pernitroso compounds, the reaction was repeated and the products examined in order to assign correct structures. The spectral properties of these compounds support the vinylnitramine structure such as (LXII) assigned to them.

The IR spectrum of (LXII) showed strong bands at 1530 and 1280 cm^{-1} due to the unsymmetrical and symmetrical stretching vibrations of the nitro group. A sharp, weak band at 1650 cm^{-1} was due to the carbon-carbon double bond stretching and the medium band at 920 cm^{-1} was due to the terminal methylene group. The NMR spectrum of the vinylnitramine also supported the structure (LXII)[60].

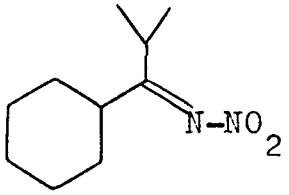
Recently, Buchi and Wuest[38] have prepared the salts of three other nitrimines (XXII), (XXIV) and (XXVIII) by treating them with potassium tert. butoxide. These salts have been formulated as N-nitroenamines (LXIII), (LXIV) and (LXV), respectively.



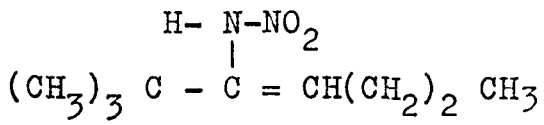
(XXII)



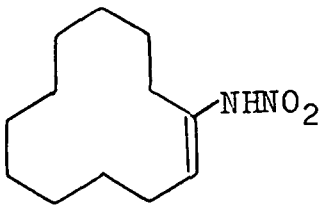
(XXIV)



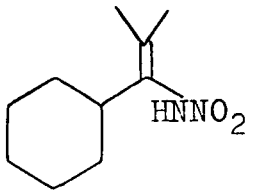
(XXVIII)



(LXIII)

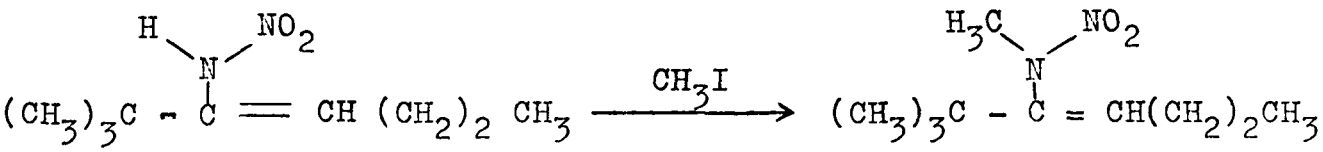


(LXIV)



(LXV)

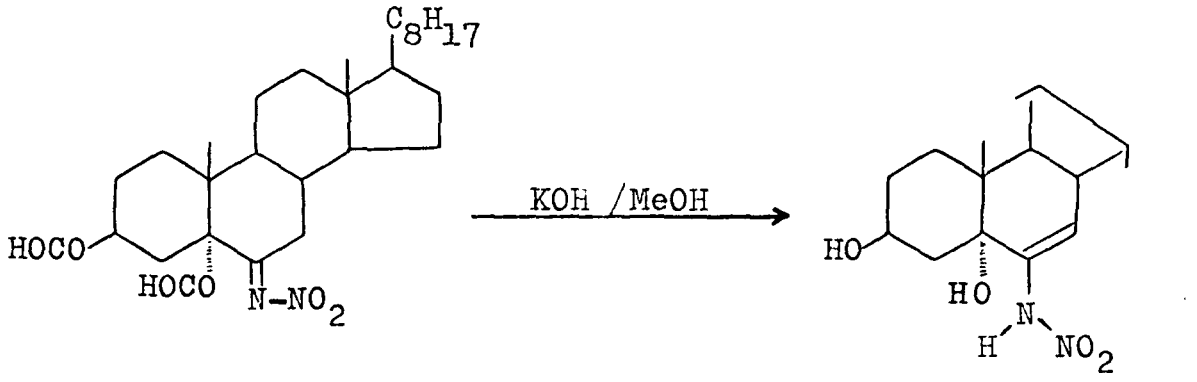
They have also carried out the methylation of nitroenamine (LXIII) with methyl iodide and obtained N-methylated-N-nitro-enamine (LXVI).



(LXIII) (LXVI)

The formulation of these compounds as N-nitroenamines is based on a comparative study of these compounds with earlier reported N-methyl-N-nitroenamine (LXII).

Suarez, et al.[56] prepared 6-nitrimino-5α-cholestane-3β-5-diol diformate (L), which on treatment with potassium hydroxide in methanol furnished isomeric 6-nitroamine-5α-cholest-6-ene-3β-5-diol (LXVII).

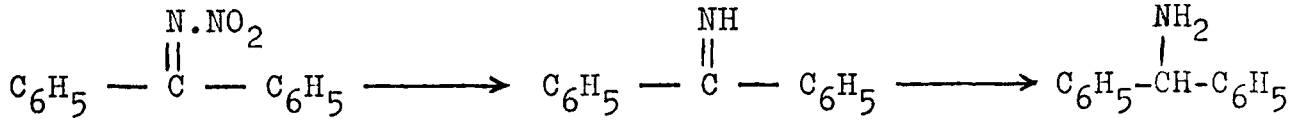


(L) (LXVII)

2. Reduction

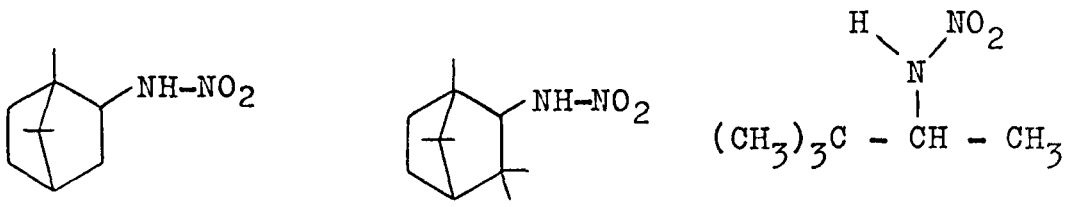
Nitrimines undergo reduction with complex metal hydrides to give nitroamines. Angelucci[24] was the first to report the reduction of pernitrosocamphor (XVI) with aluminium amalgam which produced a mixture of bornyl and isobornylamines. This result had at one time been used to argue for the existence of C —— N —— O, rather than C —— N —— N linkage in the pernitroso compounds[61].

Recently, Horner[40] has shown that the catalytic reduction of benzophenone nitrimine (LXVIII) proceeds by reduction to benzophenone imine (LXIX) and then to benzhydrylamine (LXX).



(LXVIII) (LXIX) (LXX)

Freeman[22] carried out the reduction of pernitrosocamphor (XVI), pernitrosofenchone (XVII) and pernitrosopinacolone (XVIII) with potassium borohydride in ethanol or with lithium aluminium hydride and obtained the corresponding primary amines, namely bornylnitramine (LXXI), fenchylnitramine (LXXII) and pinacolone-nitramine (LXXIII). The stereochemistry of reduction was not established so the configuration of (LXXI) and (LXXII) are unknown.

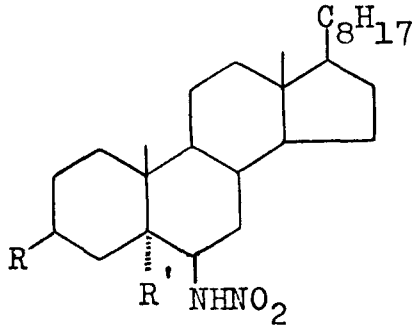


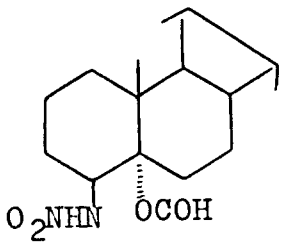
(LXXI) (LXXII) (LXXIII)

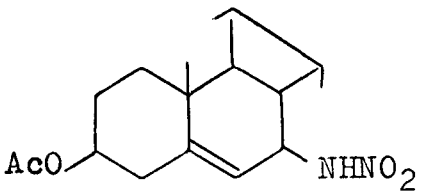
The structure of these compounds was established by elementary analysis, their IR spectra which showed N-H absorption at 3300 cm^{-1} and nitro group absorption at 1580 and 1330-1370 cm^{-1},

UV spectra which gave $\lambda_{max.}$ at 240 nm ($\varepsilon_{max.}$ 8000) and NMR spectra which exhibited the amine proton resonance.

Suarez, et al.[56], in an attempt to carry out denitroamination of steroidal nitroamines prepared some steroidal 4β-, 6β-, 7α- and 7β-nitroamines. The reduction of 6-nitrimino-5α-cholestane-3β-5-diol diformate (L), 6-nitrimino-5α-cholestan-5-yl formate (LI), 4-nitrimino-5α-cholestan-5-yl formate (LII), 6-nitrimino-5α-cholestan-3β-yl acetate (LIV) and 7-nitrimino-cholest-5-en-3β-yl acetate (LV) with sodium borohydride in absolute ethanol resulted in the saturation of the imine function to give their respective N-nitroamines, (LXXIV), (LXXV), (LXXVI), (LXXVII) and (LXXVIII).





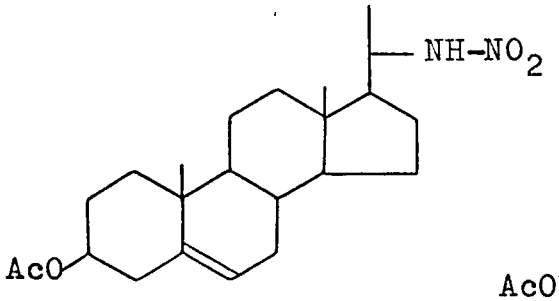


(LXXIV) R = R' = CO_2H (LXXVI) (LXXVIII)

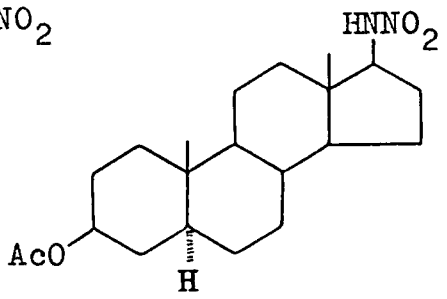
(LXXV) R = H, R' = CO_2H

(LXXVII) R = OAc, R'=H

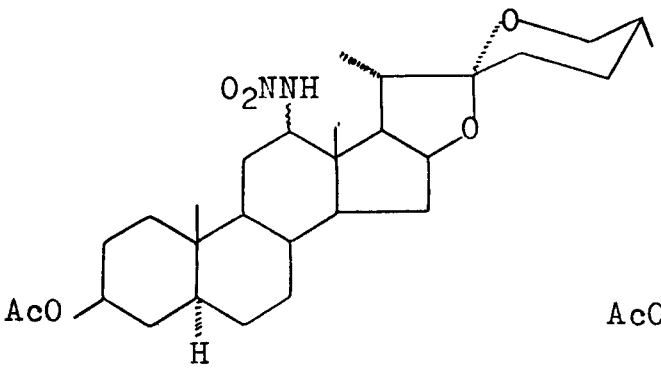
Suarez and his coworkers[57] have also obtained 20β-nitroaminopregn-5-en-3β-yl acetate (LXXIX), 17β-nitroamino-5α-androstan-3β-yl acetate (LXXX), 12β-and 12α-nitroamino (25R)-5α-spirostan-3β-yl acetate (LXXXI) and (LXXXII) and 23R-nitroamino-(20S, 22S, 25S)-5β-spirostan-3β-yl acetate (LXXXIII) by carrying out the reduction of their respective nitrimines (LVI), (LVII), (LVIII) and (LIX) with sodium borohydride in absolute ethanol.



(LXXIX)

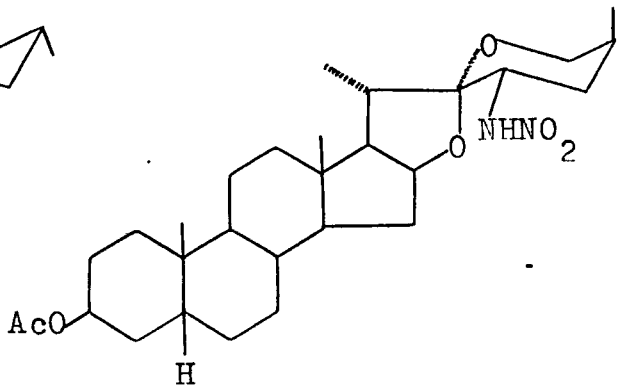


(LXXX)



(LXXXI) β-NH-NO_2

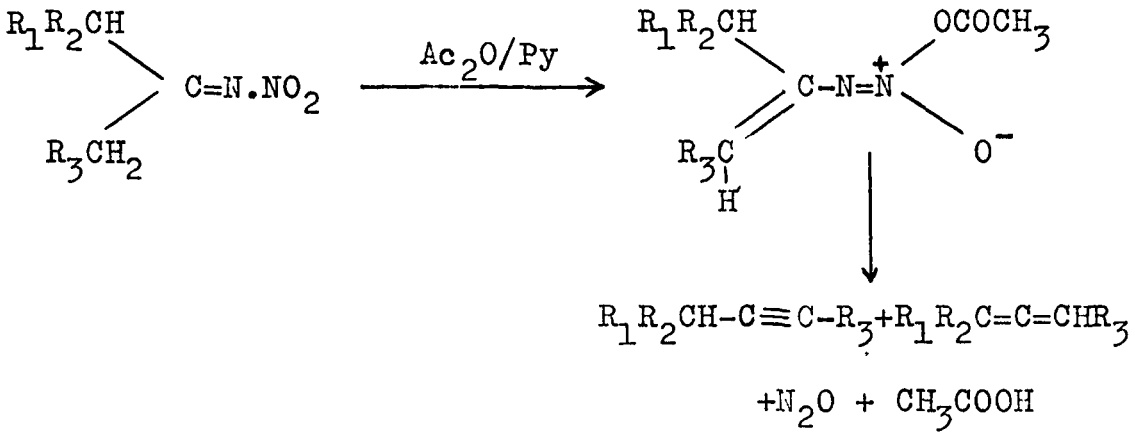
(LXXXII) α-NH-NO_2



(LXXXIII)

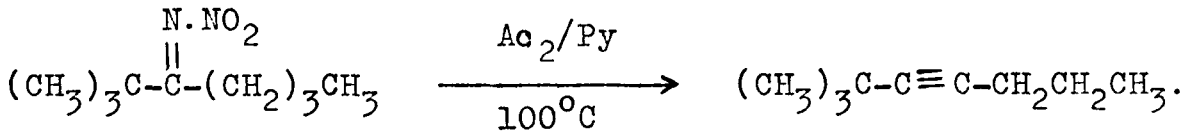
3. Transformation to Acetylenes and Allenes

Nitrimines undergo O-acylation on treatment with acetic anhydride in the presence of a base. The intermediate thus formed decomposes with the elimination of nitrous oxide and acetic acid to give acetylenes or allenes depending upon the site of deprotonation.



Similar transformation of N-nitroenamines have also been reported.

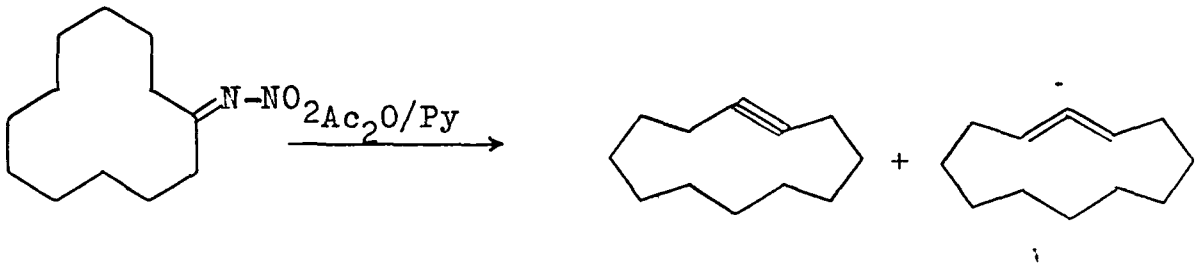
Buchi and Wuest[38] have transformed a number of nitrimines and N-nitroenamines to acetylenes and allenes by using acetic anhydride and pyridine at 100°C. In the presence of catalytic amount of 4-(dimethylamino)-pyridine[62], however, the transformation occurred at room temperature. Nitrimine (XXII), for example, when treated with acetic anhydride and pyridine at 100°C for 20 hours gave the acetylene (LXXXIV) in 65% yield.



(XXII) (LXXXIV)

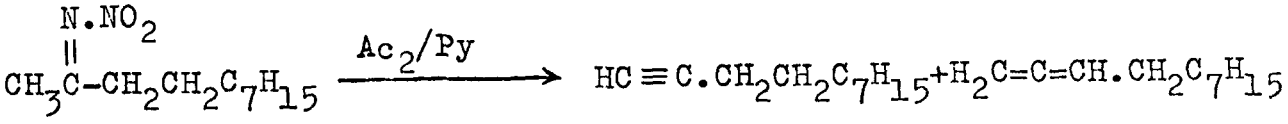
The same acetylene (LXXXIV) was obtained at room temperature when small amount of 4-(dimethylamino)-pyridine was added as catalyst to the reaction mixture.

Similarly, the nitrimine (XXIV) gave both the acetylene (LXXXV) as well as allene (LXXXVI) on treatment with acetic anhydride and pyridine at 100°C. In this case again the addition of 4-(dimethylamino)-pyridine, in catalytic amount, resulted in the formation of the same products at room temperature.

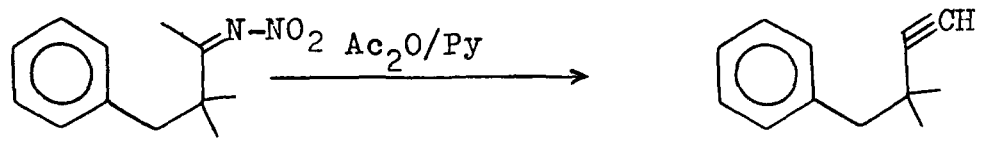


(XXIV) (LXXXV) (LXXXVI)

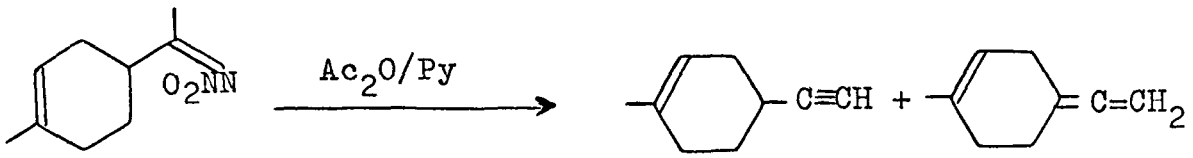
Nitrimines (XXV), (XXVI), (XXVII) and (XXVIII) also give rise to acetylenes and/or allenes when treated with acetic anhydride and pyridine.



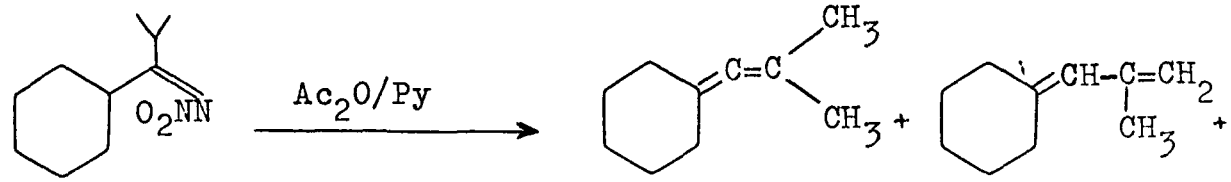
(XXV) (LXXXVII) (LXXXVIII)



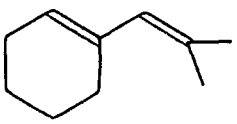
(XXVI) (LXXXIX)



(XXVII) (XC) (XCI)

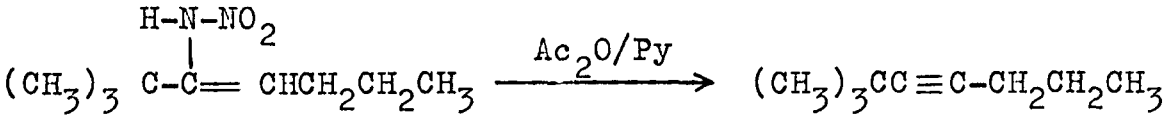


(XXVIII) (XCII) (XCIII)



(XCIV)

Buchi and Wuest[38] have also carried out the transformation of N-nitroenamine (LXIII) with acetic anhydride and pyridine and obtained the acetylene (LXXXIV).

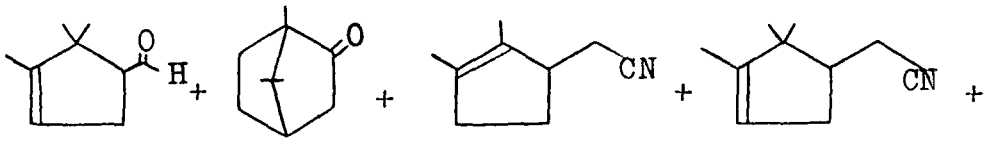


(LXIII) (LXXXIV)

It is evident from these transformations that such reactions provide a three-step dehydration of ketones to give acetylenes and allenes. This dehydration seems comparable with methods going through vinyl sulphides[63,64], and is more general than that using Hofmann elimination of quaternized enamines[65]. These reactions leading to the dehydration of ketones promise a greater synthetic value after a more widely applicable method for the preparation of nitrimines has been discovered.

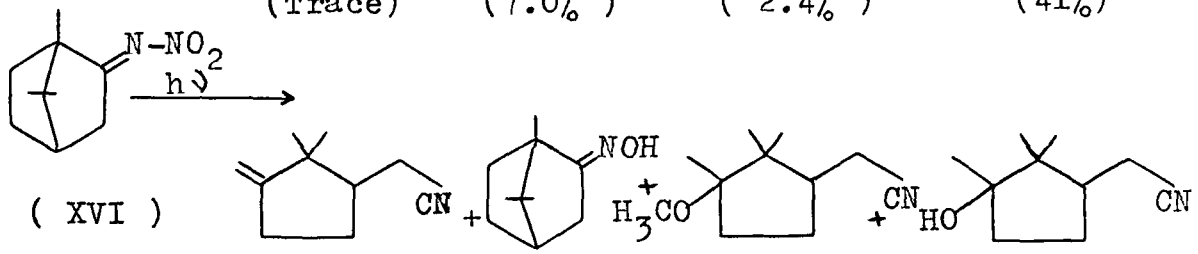
4. Photochemical and Thermolytic Transformations

Gandini[66] reported the phtochemical and pyrolytic transformations of camphornitrimine (XVI) in 1942. Winters, et al.[67] reinvestigated these transformations and obtained eight different products (XCV——CII) on photochemical transformation of camphornitrimine (XVI).



(XCV) (XCVI) (XCVII) (XCVIII)

(Trace) (7.0%) (2.4%) (41%)



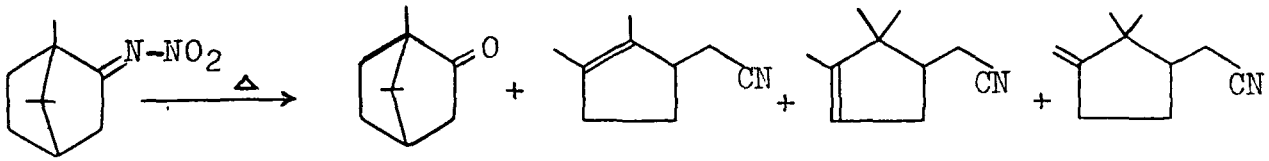
(XVI)

(XCIX) (C) (CI) (CII)

(38.6%) (Trace) (8.2%) (Trace)

The identification of compounds (XCV——C) was based on a comparable study of the retention time and IR, NMR and MS spectra with their authentic samples[66,68-70]. Compounds (CI) and (CII) were identified by their spectral properties (IR, NMR and MS).

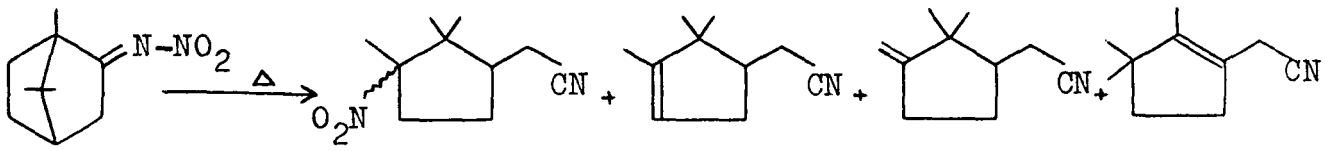
Winters, et al.[67] also carried out pyrolytic transformation of camphornitrimine (XVI) under nitrogen at 150°C for 10 seconds and obtained four different products (XCVI——XCIX).



(XVI) (XCVI) (XCVII) (XCVIII) (XCIX)

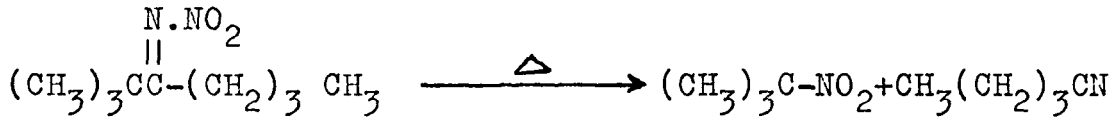
(20%) (51.6%) (Trace) (46.3%)

Recently, Buchi and Wuest[38] have carried out the pyrolysis of camphornitrimine (XVI) and obtained a mixture of epimeric nitronitrile (CIII) as the major product (38%). One of these with m.p. 74-75°C was found to be identical with a substance ($C_{10}H_{16}N_2O_2$, m.p. 57°C, typographic error) reported by Gandini[66]. In addition to the nitronitrile, they also obtained two α-campholenonitriles (XCVIII) and (XCIX) which had been reported in both the previous studies[66,67], and a β-campholenonitrile (CIV).



(XVI) (CIII) (XCVIII) (XCIX) (CIV)

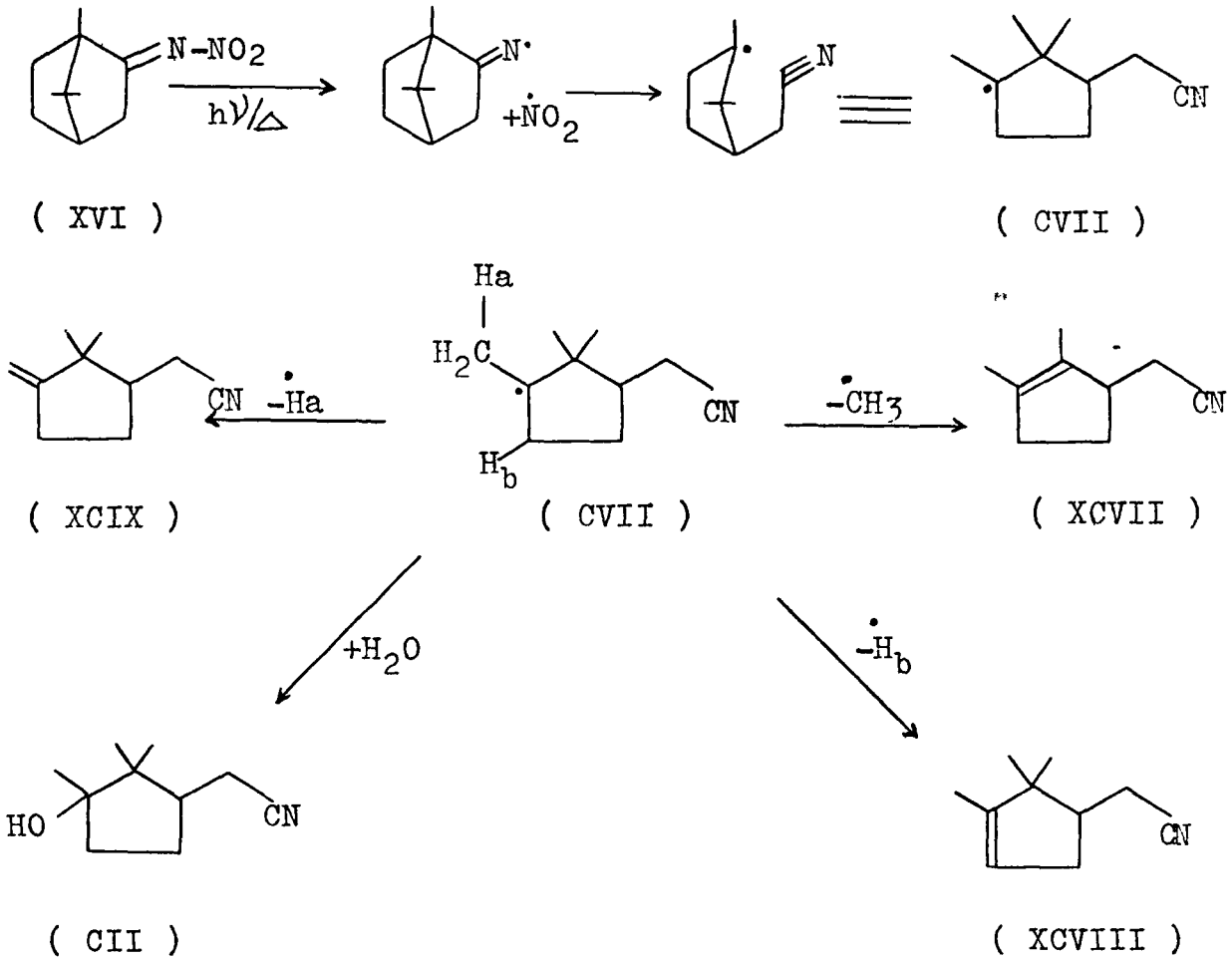
These workers[38] have also carried out the pyrolysis of 2,2-dimethyl-3-nitriminoheptane (XXII) and obtained two products characterized as 2-methyl-2-nitropropane (CV) and valeronitrile (CVI).



(XXII) (CV) (CVI)

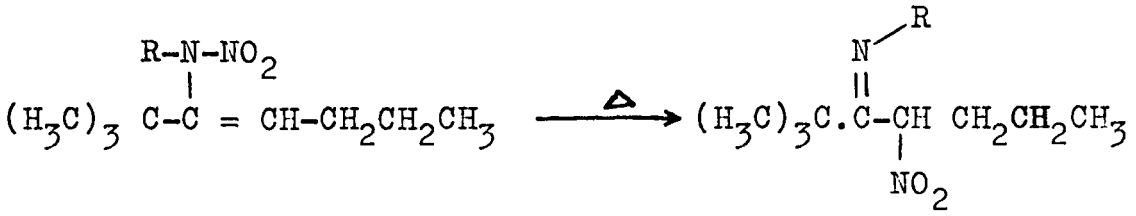
The nature of the products obtained on photochemical and pyrolytic transformations of nitrimines led Winters, et al.[67] to propose that the first step in these reactions is the homolytic cleavage of $N-NO_2$ bond and subsequent generation of radical (CVII). This radical then rearranges differently to give appropriate products (Scheme 7).

Scheme 7



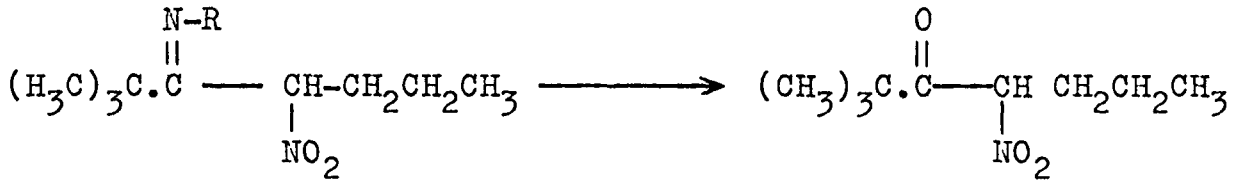
The abstraction of a hydrogen atom by the NO_2 radical would also produce nitrous acid which may break up to form NO, NO_2 and H_2O. These products have been identified and measured[66]. The reaction of water with the radical (CVII) would probably lead to the formation of (CII). The aldehyde (XCV) is most likely formed from camphor by secondary photolysis[70]. No mechanisms for the formation of (XCVI), (C) and (CI) have been suggested.

Buchi and Wuest[38] have reported the thermolytic transformation of some N-nitroenamines and have obtained α-nitroimine as the major product. The N-nitroenamine (LXIII), for example, gave 2,2-dimethyl-4-nitro-3-iminoheptane (CVIII) on thermolysis in xylene. Similar treatment of N-methyl-N-nitroenamine (LXVI) gave the α-nitroimine (CIX).



(LXIII)	R,H	(CVIII)	R,H
(LXVI)	R,CH_3	(CIX)	R,CH_3

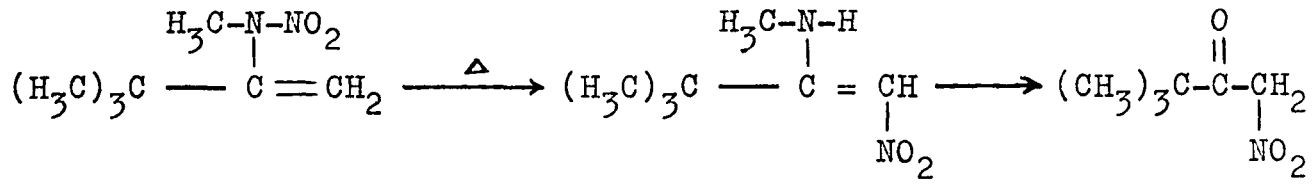
Both these α-nitroimines (CVIII) and (CIX) on hydrolysis over wet silica gel in benzene led to the formation of the same α-nitroketone (CX).



(CVIII) R,H

(CIX) R,CH_3

Similarly, N-methyl-N-nitroenamine (LXII) derived from pinacolone also rearranges thermally to give the C-nitro isomer in its enamine form (CXI) which is hydrolysed to α-nitroketone (CXII).



(LXII) (CXI) (CXII)

The α-nitroketones prepared by the thermal rearrangement of the N-nitroenamines and the hydrolysis of α-nitroimines, were in good agreement with the data collected on other α-nitroketones[71,72].

PART - THREE

MASS SPECTRAL STUDIES ON NITRO COMPOUNDS

In recent past, mass spectrometry has developed to become a very powerful analytical tool of an organic chemist's arsenal. The structure determination of almost every class of organic compounds, has been aided by this technique which combines unique structural identification capabilities with high sensitivity. The diagnostic electron-impact induced breakdown patterns, characteristic of different functionalities, have made it indispensable to chemists.

The mass spectrometric study of nitro compounds has been a very productive area of research and in recent years a tremendous effort has been put forth on investigation with this technique. Various groups of workers have carried out intensive study of the mass spectrometric fragmentation of a variety of nitro compounds. As a result of these studies useful correlations between spectra and structures have been established.

During the last two decades, the mass spectra of several aliphatic, alicyclic and aromatic nitro compounds have been measured by low as well as high resolution techniques. The characterization of aliphatic nitro compounds by mass spectrometry is complicated in most cases by the lack of discernible molecular ions, with the notable exception of nitromethane. The nitro

group is not a favourable charge-stabilizing centre directing further fragmentation. This fact is explained by the occurrence to only a very minor extent of any product resulting from the McLafferty rearrangement. One of the most important processes in the mass spectrometry of nitro compounds is the loss of an NO_2 radical and the subsequent decomposition of alkyl fragment. Another equally important process is the loss of both the oxygen atoms, apparently by the sequential elimination of an oxygen and of water, to yield the equivalent of nitrile species. Rearrangement of an oxygen atom with the generation of ions containing only C,H and O is of no importance in nitroalkanes. The loss of the elements of HNO_2 and the subsequent decomposition of the resulting olefins represent the most significant feature of the mass spectra of tertiary nitroalkanes. The mass spectra of aromatic nitro compounds show evidence for the primary loss of O, NO and NO_2 and for formation of $\overset{+}{NO}$. Derivatives with an ortho substituent containing α-hydrogens show loss of $\dot{OH}$ rather than O; such loss of OH is often followed by the loss of CO.

The mass spectrum of nitromethane (CXIII)[73] is quite simple. An abundant molecular ion is accompanied by CH_3^+, NO_2^+ and $\overset{+}{NO}$ ions, representing the most important daughter ions. The loss of an oxygen atom to give $CH_3\overset{+}{NO}$ (m/z 45) is of minor importance. The spectrum, however, becomes more and more complicated as we go to the higher homologues of nitromethane. In the nitroethane

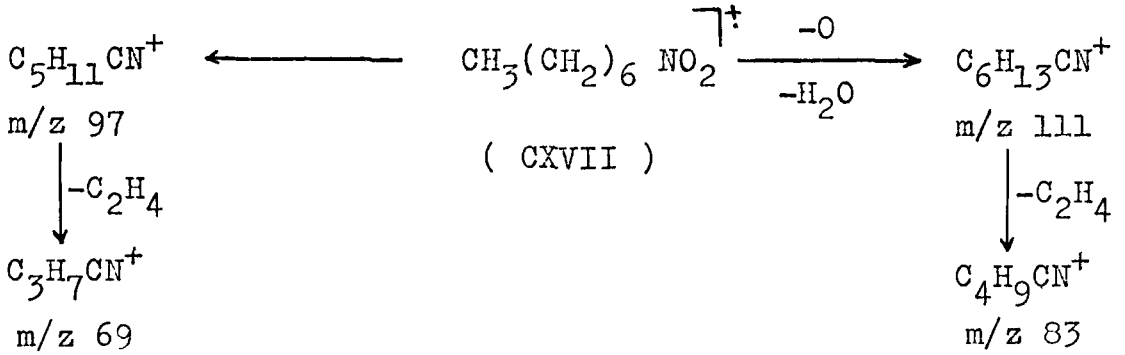
(CXIV)[73] spectrum the molecular ion is of low intensity and it becomes indiscernible in the spectra of higher nitroalkanes. α-Cleavage, an important feature with alkyl nitrite[74] is essentially absent in the case of nitroalkanes. The fragment ions corresponding to those observed in nitromethane become less and less important with increasing molecular weight. The mass spectra of isomeric nitroalkanes are quite similar and differ only in the relative abundance of some fragment ions. The abundance of NO_2^+ ion (m/z 46) decreases as we proceed from nitromethane to its higher homologues. The NO^+ ion (m/z 30), which is responsible for the base peak in the spectrum of nitromethane (CXIII), declines gradually in its importance with increasing molecular weight.

$CH_3.NO_2$	$CH_3CH_2.NO_2$	$CH_3CH_2CH_2.NO_2$	$CH_3\underset{\displaystyle NO_2}{\underset{\vert}{C}}HCH_3$
(CXIII)	(CXIV)	(CXV)	(CXVI)

The hydrocarbon fragments which can be found in the spectra of functional derivatives of alkanes[75] also play an important role in the spectra of nitroalkanes. One of the most important fragments in the spectrum of nitroethane (CXIV) is the $C_2H_5^+$ ion (m/z 29) which may decompose further to $C_2H_3^+$ (m/z 27). Similarly in the spectra of 1- and 2-nitropropanes (CXV) and (CXVI) respectively, $C_3H_7^+$ (m/z 43), $C_3H_5^+$ (m/z 41), $C_3H_3^+$ (m/z 39),

$C_2H_4^+$ (m/z 28) and $C_2H_3^+$ (m/z 27) belong to the most outstanding fragment ions. It can thus be concluded from these observations that the loss of an NO_2 radical to yield the appropriate $(C_nH_{2n+1})^+$ ion is a prominent process and could be of diagnostic value. But since the higher alkyl ions are very prone to decompose further, especially to the very stable C_3 and C_4 fragments, the abundance of $(M-NO_2)^+$ species becomes very low with increasing chain length.

The most interesting feature of the mass spectra of nitroalkanes is the occurrence of oxygen free C H N fragments. They start formally with HCN, but higher homologues may also be observed. The formation of CH_3CN^+ in nitroethane (CXIV) could be established as the loss of oxygen atom followed by the elements of water as indicated by a metastable ion for the transition m/z 59 ⟶ m/z 41 (calculated 28.5, found 28.6). The resulting nitrile ions decompose further, preferentially by the expulsion of ethylene. This is illustrated in the mass spectrum of nitroheptane (CXVII) by the high abundance of $C_4H_9CN^+$ (m/z 83), as compared with $C_3H_7CN^+$ (m/z 69) and $C_5H_{11}CN^+$ (m/z 97), and the presence of a metastable ion for transition m/z 97 ⟶ m/z 69 (calculated and found 49.1).

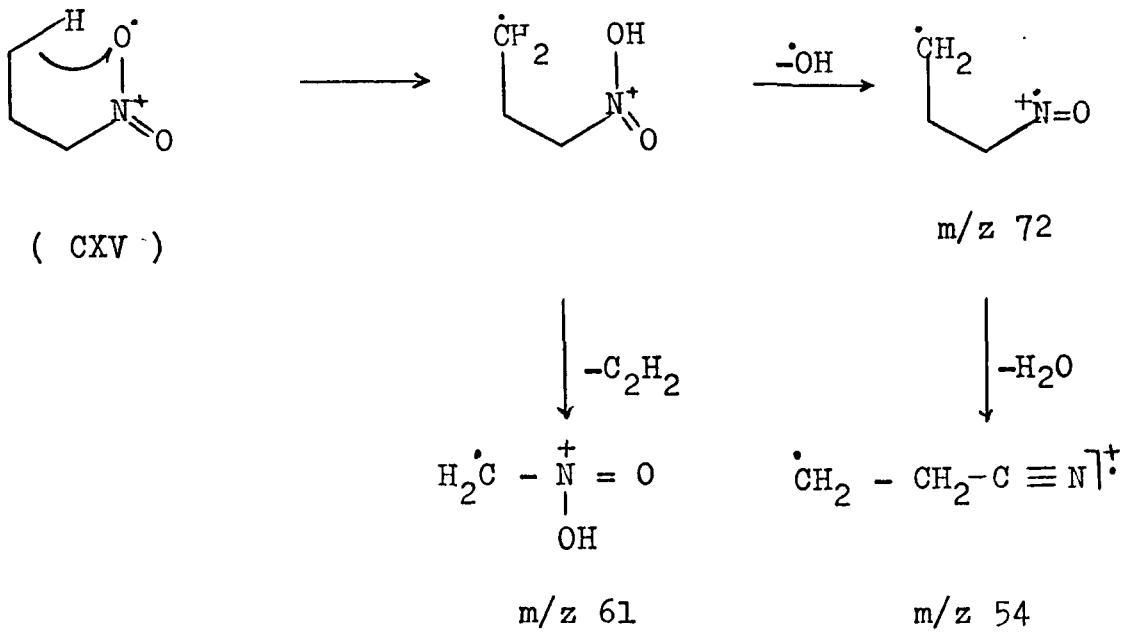


A detailed examination of the mass spectra of 1-nitropropane (CXV) and specifically deuterated analogues[76] (CXV a-c) has been carried out in an attempt to rationalize the genesis of different fragment ions in nitroalkanes. These spectra have revealed that very small M^+-OH (m/z 72) and $M^+-C_2H_4$ (m/z 61) peaks appear in the high mass ranges and the genesis of both the ions involves specific γ-hydrogen transfer reactions as evidenced by the M^+-OD (m/z 74) and $M^+-C_2D_2H_2$ (m/z 62) peaks in the spectrum of (CXV a).

$CH_3CH_2.CH_2.NO_2$	$CH_3CH_2CD_2NO_2$	$CH_3CD_2CH_2NO_2$	$CD_3CH_2CH_2NO_2$
(CXV)	(CXVa)	(CXVb)	(CXVc)

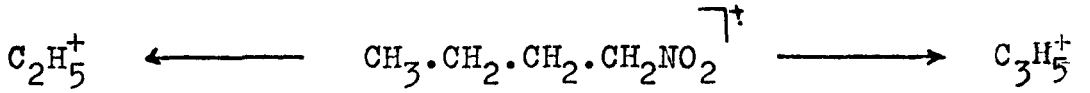
These facts can be accommodated by the sequence shown in scheme 8. In addition, the fragment ion of mass 54 can arise by the loss of water from the ion m/z 72. The deuterium labelling establishes that both α-hydrogens are eliminated in this process and hence a nitrile (m/z 54) may be formed. Since the α-labelled nitropropane (CXVa) loses only D_2O in going to m/z 54, a cyclic structure for m/z 72, in which the α- and γ-CH_2 groups become equivalent, is excluded.

Scheme - 8



The most abundant ions in the spectrum of nitropropane (CXV) are associated with $C_2H_3^+$, $C_3H_5^+$ and $C_3H_7^+$ at m/z 27, 41 and 43, respectively. The similarity of the spectra of deuterated analogues (CXVa) and (CXVb) upto m/z 45 has led to the suggestion[74] that the propyl cation ($C_3H_7^+$) from (CXVa) and (CXVb) can become equivalent through a 1,2 methyl shift. If such a shift occurs, then the decomposition of the deuterated propyl cation from (CXVa) and (CXVb) to alkyl cations can proceed through loss of H_2 and HD whereas the γ-deuterated cation should predominantly eliminate HD, as observed.

The mass spectrum of nitrobutane (CXVIII) largely affords abundant hydrocarbon ions[73] such as $C_4H_9^+$, $C_3H_5^+$ and $C_2H_5^+$ and gives fragment ion peaks at m/z 57, 41 and 29 respectively.

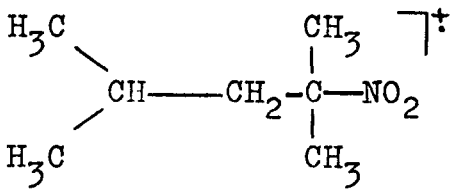


m/z 29 m/z 41

(CXVIII)

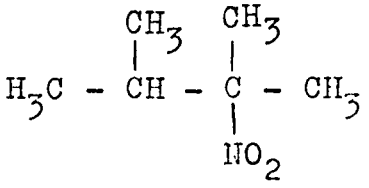
m/z 57

The mass spectra of several tertiary nitroalkanes[73], such as 2,3-dimethyl-2-nitrobutane (CXIX) 2,4-dimethyl-2-nitropentane (CXX) and 2,4,4-trimethyl-2-nitropentane (CXXI) have been examined. The main feature is the loss of HNO_2 from the molecular ion giving the highest discernible peak in the various spectra. The subsequent fragmentation pattern of (CXX) corresponds to the combination of the decomposition modes of two olefins (m/z 98)with the exception of an abundant NO^+ (m/z 30) ion and a small amount of CH_3CN^+ (m/z 41) ion.

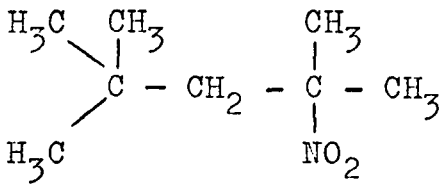


(CXX)

m/z 98 m/z 98

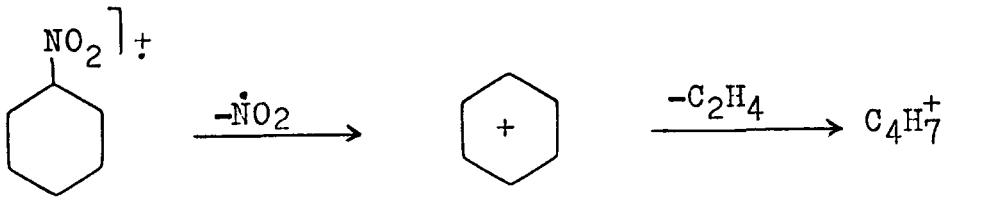


(CXIX)



(CXXI)

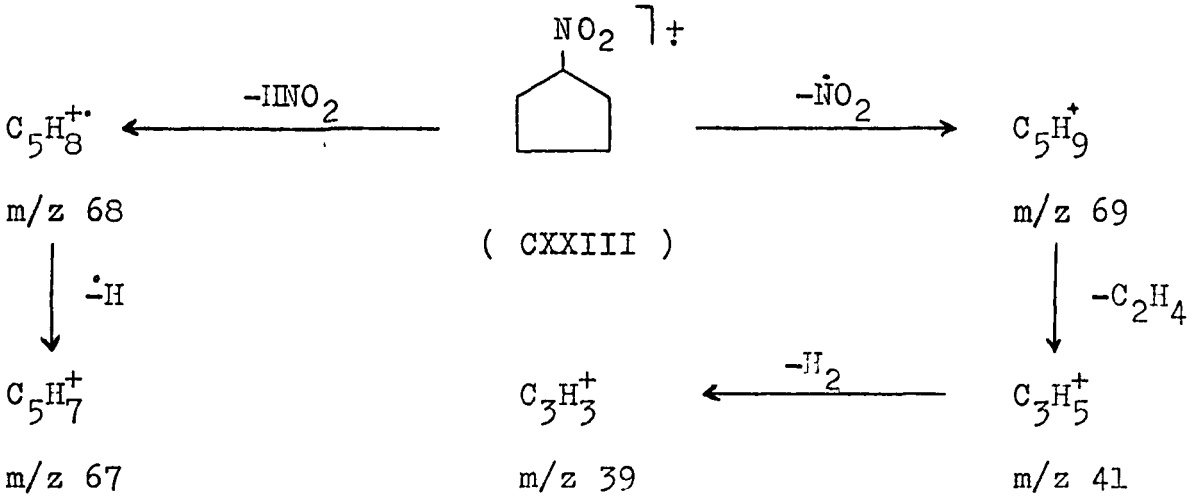
The mass spectra of some alicyclic nitro compounds[73] have been examined. In nitrocyclohexane (CXXII) an ion formed by the loss of NO_2 is responsible for the highest intense peak at m/z 83 representing the cyclohexyl ion. The cyclohexyl ion decomposes further by the expulsion of ethylene to give $C_4H_7^+$ (m/z 55). This transition is supported by a metastable ion peak at m/z 36.5. The spectrum of nitrocyclohexane (CXXII) also contains a series of additional hydrocarbon ions.



(CXXII) m/z 83 m/z 55

The mass spectrum of nitrocyclopentane (CXXIII) is less complicated. The loss of NO_2 gives a peak at m/z 69 ($C_5H_9^+$) which subsequently eliminates C_2H_4 to give a peak at m/z 41 ($C_3H_5^+$) and further elision of two hydrogen atoms gives yet another peak at m/z 39 ($C_3H_3^+$). The two transitions, i.e., m/z 69 ⟶ m/z 41 and m/z 41 ⟶ m/z 39 are supported by metastable ions at m/z 24.4 and 37.2, respectively. In addition, there occurs the loss of HNO_2 to give a daughter ion at m/z 68

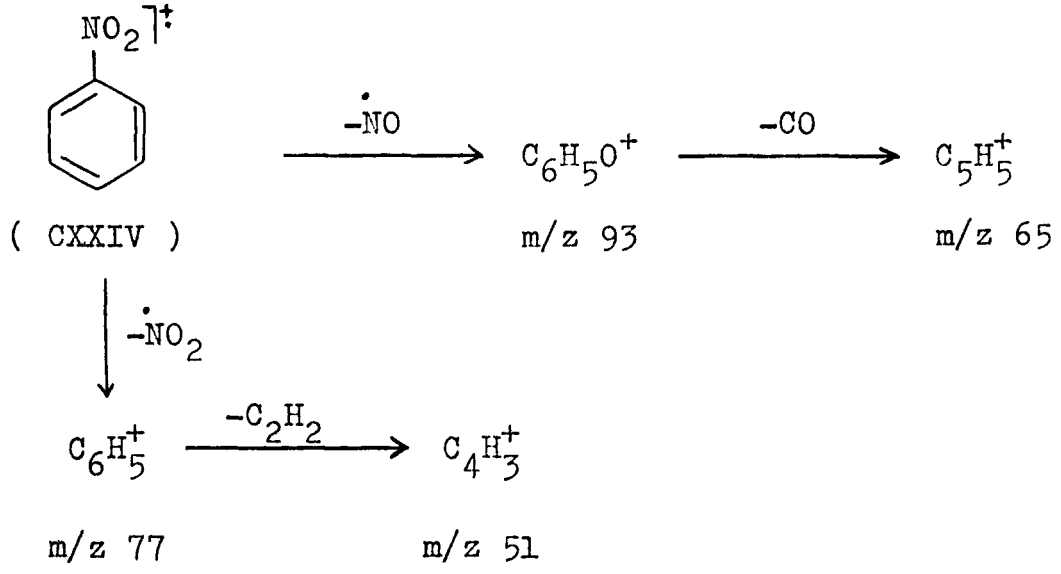
($C_5H_8^+$) with the resulting cyclopentene ion losing an additional hydrogen atom to give a peak at m/z 67 ($C_5H_7^+$). A metastable ion at m/z 66.2 supports the transition m/z 68 ⟶ m/z 67.



The mass spectra of aromatic nitro compounds show evidence for the primary loss of O, NO and NO_2 and for the formation of NO^+. Derivatives with an ortho substituent containing α-hydrogens such as CH_3, NH_2 or OH, show the primary loss of OH rather than O. Such loss of OH is often followed by the loss of CO. The pronounced effects of ortho substitution on the mass spectra of nitroarenes are probably related to wide range of poorly understood reactions displayed by ortho substituted nitroarenes in more conventional chemical and photochemical systems.

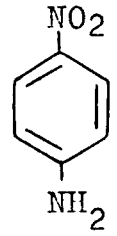
The mass spectrum of simplest nitroarene, namely nitrobenzene (CXXIV)[77] reveals an intense molecular ion peak while the base peak corresponds to $C_6H_5^+$ (m/z 77), due to the

loss of the nitro substituent. A metastable ion peak demonstrates the further elimination of an acetylene molecule with production of $C_4H_3^+$ (m/z 51) ion. The most interesting fragment is the one of mass 93, resulting from a rearrangement with the loss of NO in a one-step process. The rearrangement may involve isomerization to the nitrite form prior to the fragmentation[78]. The m/z 93 ion thus corresponds to the phenoxy cation ($C_6H_5^+O$) from which the $C_5H_5^+$ (m/z 65) arises by ejection of CO. The effect of electron-withdrawing and donating meta-and para-substituents upon the formation of the two ions, $\dot{M}^+$-NO and $\dot{M}^+$-(NO + CO) has been studied[79] in detail by using the techniques of Hammet plots and 'flat topped' metastable ions energy calculations.

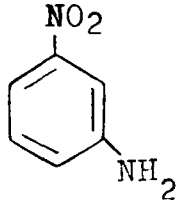


The mass spectra of isomeric nitroanilines have been discussed[80-82] by taking into consideration the occurrence of metastable peaks and accurate mass measurements. In the upper

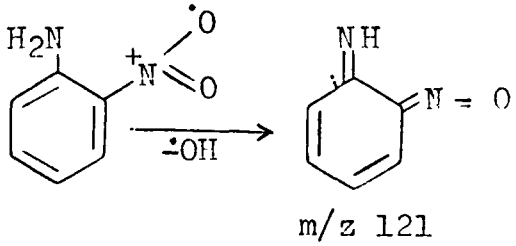
mass range p- and m-nitroanilines (CXXV) and (CXXVI), respectively, show the loss of oxygen from the molecular ion while the o-isomer (CXXVII) exhibits the loss of hydroxyl radical from the molecular ion. A six-membered transition state has been proposed[83] to account for the loss of a hydroxyl radical and has been substantiated by deuterium labelling, which also uncovered the operation of a strong isotope effect for this process.



(CXXV)



(CXXVI)



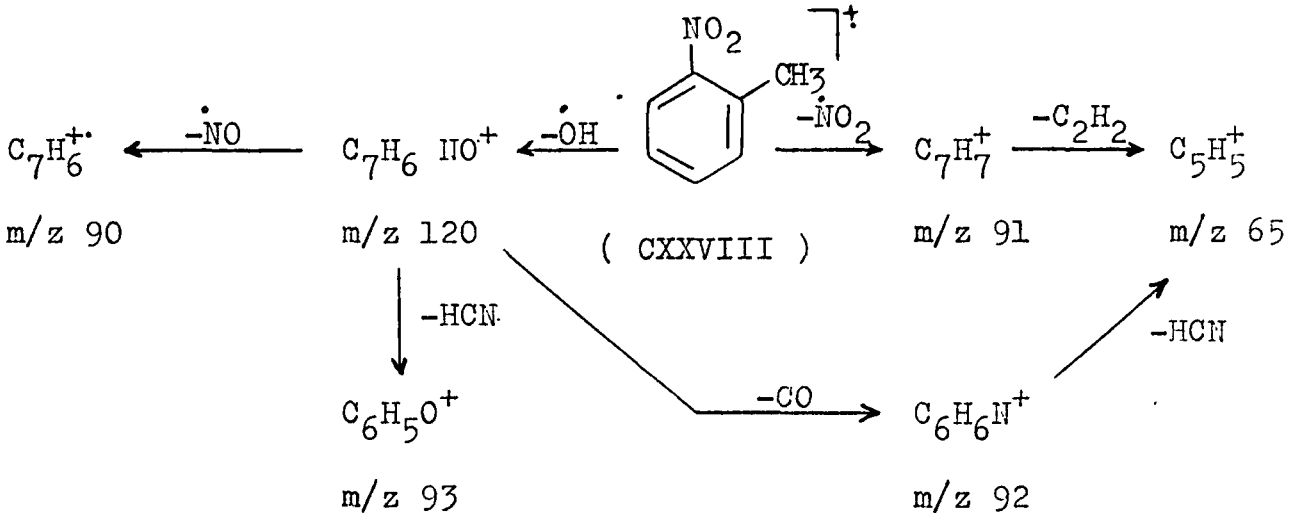
m/z 121

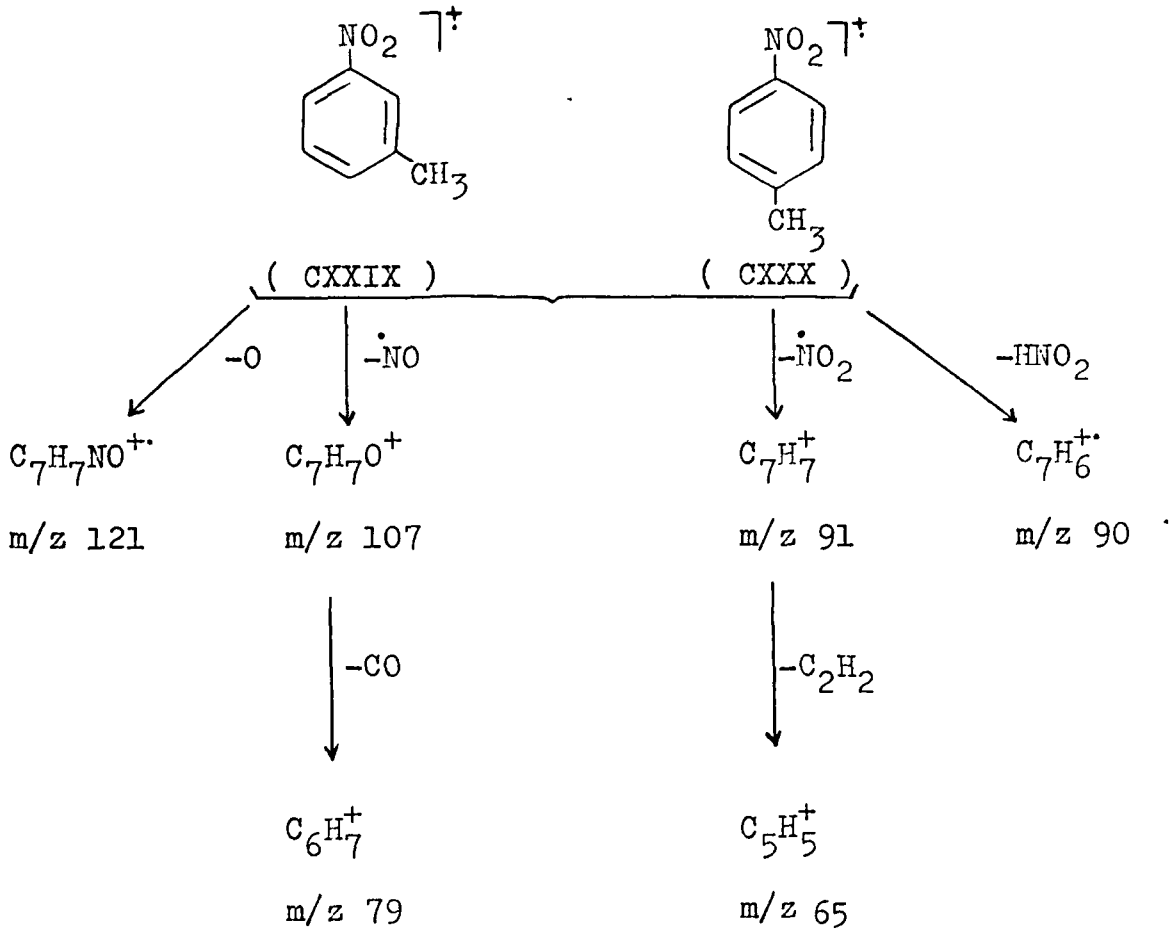
(CXXVII)

The substituent effect on the mass spectra of nitroarenes has been best exemplified by the reference to isomeric nitrotoluenes.

In the spectrum of o-nitrotoluene (CXXVIII)[84], intensities at the (M^+-17), (M^+-44), (M^+-45) and (M^+-47) units are higher and those of the molecular ion (M^+), (M^+-16), (M^+-30), (M^+-46) and (M^+-58) are lower than in their meta-and para-isomers (CXXIX) and (CXXX), respectively. These contrasting patterns as well as metastable peaks hint to gross differences in the underlying chemistry. The most abundant primary reaction product in the spectrum of o-nitrotoluene (CXXVIII) arises by the loss of OH, which may be followed by loss of either CO or HCN. The

competition from this group of reactions evidently reduces the yields of products from the primary loss of O, NO and NO_2. The fragment ion formed by the loss of mass unit 58 from the molecular ion, apparently arises by sequential loss of NO and CO. The spectra of the m- and p-nitrotoluenes show essentially nothing corresponding to the primary loss of OH and associated secondary reactions. The difference in intensity of the (M^+-47) daughter ion, coupled with the appreciable intensities at this mass in all the three spectra suggests that the peak includes contributions from two separate processes:in one, the elements of HNO_2 are lost as a unit or possibly as NO_2 and H; in the other, they are lost in two steps as OH and NO.



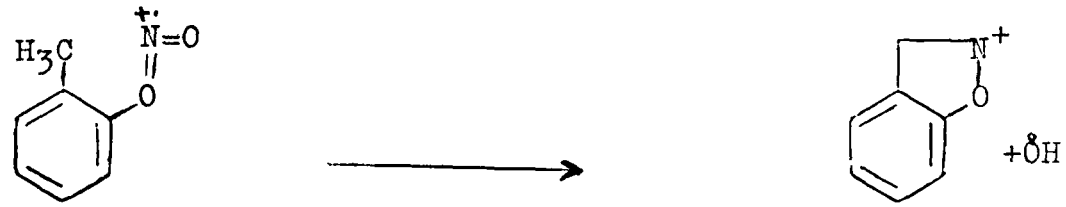


The above observation consitutes strong circumstantial evidence that the hydrogen atom lost as OH from the ortho isomer comes from the methyl group and this inference is confirmed by the spectrum of α-d-species. A deuterium atom in the methyl group opposses the primary loss of OH to form $C_7H_6NO^+$ and also stabilizes this ion, once formed, against further decomposition to $C_6H_5O^+$. It was found that the label retention in $C_7H_6NO^+$ is 81%, substantially higher than the 67% that would be expected on a purely random statistical basis. Thus, the observed yield of this ion reflects the

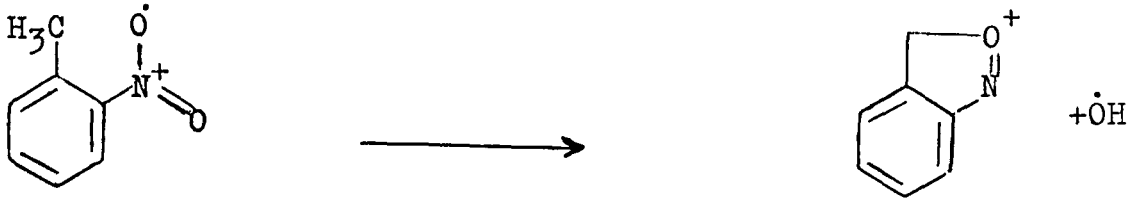
counterbalancing effects of an increase in the strength of the C-D bond and weakening of the methyl C-H bonds compared with the corresponding bonds in the unlabelled molecules[85,86].

In labelled p- nitrotoluene there is no isotope effect on the intensities of $C_7H_7NO_2^+$, $C_7H_7NO^+$, $C_7H_7O^+$, $C_6H_7^+$ and probably $C_5H_5^+$. The absence of the isotope effect is consistent with the postulated decomposition reaction, none of which requires cleavage of a methyl C-H bond except for the presumed ring expansion step in which $C_7H_7^+$ attains the symmetrical tropylium configuration. In the meta isomer also, spectral intensities of the labelled species parallel closely those of the unlabelled species, with no suggestion of isotopic effect.

Beynon, et al.[87] have carried out a detailed study on the dissociation pattern of o-nitrotoluene (CXXVIII) and have observed significant ortho effect. They obtained the most abundant ion in the spectrum at m/z 120 due to the loss of OH from the molecular ion which could possibly arise in two different ways. If the molecular ion undergoes rearrangement to the isomeric nitrite form before dissociation, as it presumably does in the reactions characteristic of nitroarenes, it is envisaged that the loss of OH occurs as in scheme-9a. Alternatively, if the nitro group retains the configuration usually associated with the neutral molecule, then dissociation may be considered to proceed as in scheme-9b.

(a) 

m/z 120

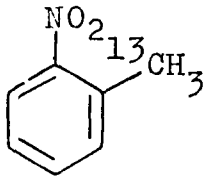
(b) 

m/z 120

The ion m/z 120 can be shown to dissociate further by losing CO to form the ion m/z 92. A metastable peak at m/z 70.5 supports this transition. The carbon atom of the CO group ejected in this fragmentation could be derived either from the methyl group or from the benzene ring, depending upon which of the two fragmentation routes postulated above is responsible for the formation of m/z 120 ion. In an attempt to distinguish between the two possibilities, isotopically labeleed o-nitro $Me^{13}C$ toluene (CXXXI) was prepared and its mass spectrum obtained. It is evident from the compound (CXXXI) that if the carbon of the CO group comes from the ring then the peak at m/z 92 should shift to m/z 93 and the molecular ion must undergo

rearrangement to the nitrite form before undergoing any fragmentation. Conversely, if the peak at m/z 92 is not shifted to m/z 93, then the carbon atom must be derived from the methyl group and the molecular ion does not undergo any rearrangement.

The labelled compound could not be produced in a pure state. It was actually produced in 54% concentration in admixture with unlabelled o-nitrotoluene. The spectra of this mixture and of the unlabelled compound were obtained by substraction of one spectrum from the other.

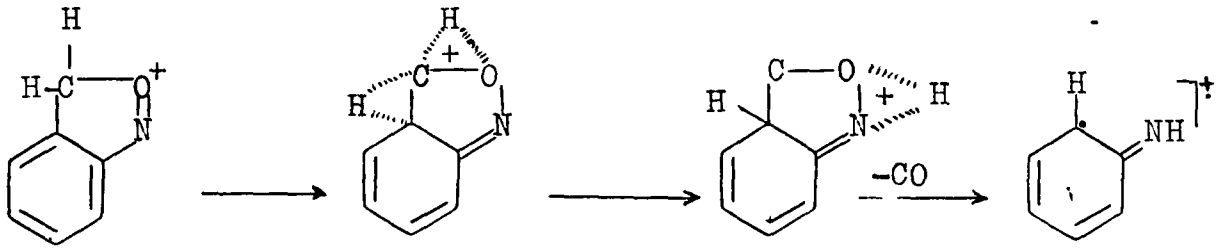


(CXXXI)

It was clear from a study of the results that the major contribution to the M^+-(OH+CO) ion in the spectrum of the labelled compound (CXXXI) was due to $C_6H_6N^+$ ion (m/z 92) and only a small contribution is noted at m/z 93 ($C_5^{13}CH_6N^+$). Therefore, the major fragmentation mode that results in the loss of CO from the (M^+-OH) ion involves the loss of carbon from the methyl group.

It is difficult to postulate a precise mechanism whereby this product ion is formed, or to visualize the transition states involved in transferring the two hydrogen atoms from the methyl group, but it seems possible that one of the hydrogens will transfer to the adjacent ring carbon while the other transfers to the nitrogen via the oxygen atom as shown in scheme 10.

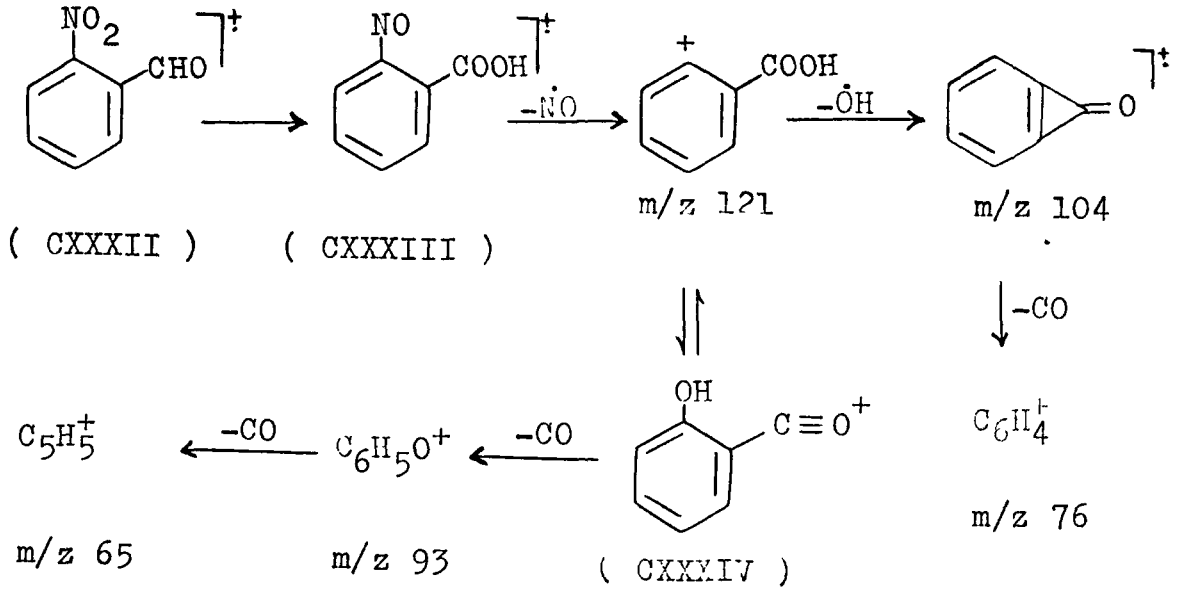
Scheme - 10



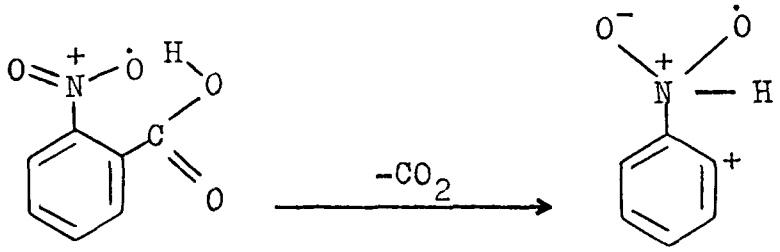
m/z 92

A number of nitro compounds in which a carbonyl group is present in the ortho position have been examined. The spectra of their deuterated derivatives have been used to aid the interpretation. Generally speaking in these compounds the $M-NO_2$ ions, which are so abundant in nitrobenzene and its derivatives[78], are of small or negligible abundance. The process of α-cleavage adjacent to the carbonyl group[88] gives rise to the base peak in the spectra of most of these compounds.

Many aromatic nitro compounds exhibit (M^+-NO) peaks in their spectra[78]. This fragmentation mode necessitates a rearrangement process, probably to the nitrite form, in the molecular ion in most cases. In the mass spectrum of o-nitrobenzaldehyde (CXXXII), the (M^+-NO) ion at m/z 121 ($C_7H_5O_2^+$) corresponds to the base peak. Evidently the presence of an ortho aldehyde group facilitates the expulsion of NO, perhaps from the rearranged product o-nitrosobenzoic acid (CXXXIII). An analogous high yield photochemical rearrangement has long been known[89]. A rearrangement in this (M^+-NO) ion can afford the isomeric o-hydroxybenzoyl cation (CXXXIV) which might then be expected to decompose by successive loss of CO molecules to $C_6H_5O^+$ and $C_5H_5^+$, exactly as observed and substantiated by metastable ion peaks. Alternatively, the loss of a hydroxyl radical from m/z 121 could lead to a benzcyclopropenone ion radical (m/z 104) and thence by loss of CO to a benzyne ion radical (m/z 76). A similar decomposition to a benzyne ion radical via a benzcyclopropenone seems to be operative in the mass spectra of many naphthaquinones[90].

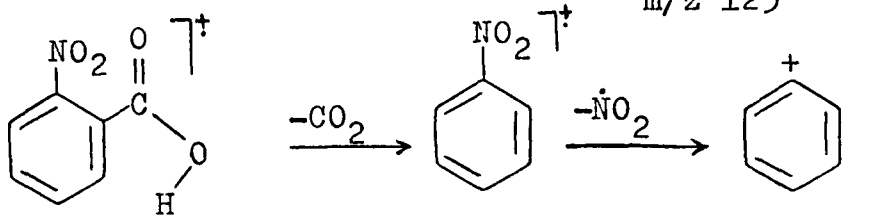


The mass spectrum of o-nitrobenzoic acid (CXXXV)[91] contains a pronounced fragment ion peak at m/z 123 ($C_6H_5NO_2^+$), due to a decarboxylation reaction induced by electron-impact. The process occurs to a negligible extent in the breakdown of m- and p-nitrobenzoic acids (CXXXVI) and (CXXXVII), respectively. Therefore, it appears likely that the decarboxylation reaction is not reliant upon the mesomeric effect of a nitro group, but rather upon its inductive effect or upon the direct interaction of the ortho substituent through space. Hence rearrangement of the carboxylic acid hydrogen atom to nitrogen or directly to the aromatic nucleus may be entertained. The sequence in which the carboxylic acid hydrogen atom directly migrates to the aromatic nucleus appears more likely since part of the spectrum below m/z 123 is similar to that of nitrobenzene.

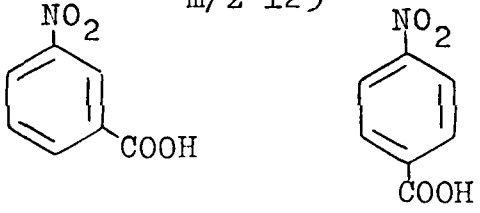


(CXXXV)

m/z 123

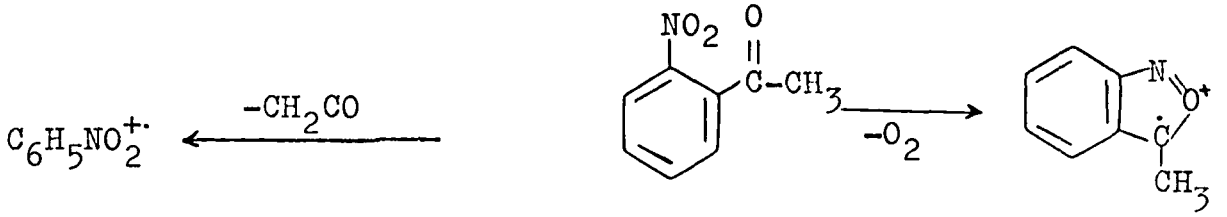


(CXXXV) m/z 123 m/z 77



(CXXXVI) (CXXXVII)

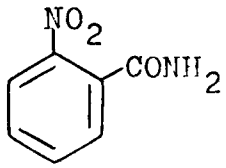
The mass spectrum of o-nitroacetophenone (CXXXVIII)[91] contains a fairly abundant m/z 123 ion ($C_6H_5NO_2^+$) which arises via elimination of ketene from the molecular ion. It can definitely be stated that this ion does not have the same structure as nitrobenzene molecular ion, since it does not decompose by elimination of NO to m/z 93 and the spectrum contains a fragment ion corresponding to the benzyne ion radical (m/z 76) which is much more abundant than that corresponding to the phenyl cation (m/z 77). Hence a hydrogen migration to nitrogen is indicated in this case. The fragment ion m/z 123 can then decompose by loss of HNO_2 to the benzyne ion radical. The mass spectrum of o-nitroacetophenone (CXXXVIII) is remarkable for the presence of an (M^+-O_2) species, which is due to the $C_8H_7NO^+$ ion radical (m/z 133) plausibly represented as 3-methylanthranil ion radical (CXXXIX) which contains a completely delocalized system.



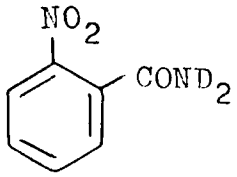
m/z 123 (CXXXVIII) (CXXXIX) m/z 133

The mass spectrum of o-nitrobenzamide (CXL)[91] has been interpreted by use of high resolution measurements and of the spectrum of N-d_2 derivative (CXLI). The peaks at m/z 75 ($C_6H_3^+$),

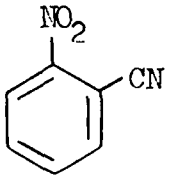
76 ($C_6H_4^+$), 90 ($C_6H_4N^+$), 102 ($C_7H_4N^+$), 118 ($C_7H_4NO^+$) and 148 ($NO_2C_6H_4CN^+$) are temperature variable and arise from the decomposition of the nitrile (CXLII) which is produced by thermal dehydration. The spectrum of the nitrile (CXLII) does not uncover any ortho effect. In the spectrum of d_2-derivative of o-nitrobenzamide (CXX), the major portion of peak at m/z 118 is shifted to m/z 120 and is shown by the exact mass measurement to be due to an M-30 species ($C_7H_6NO_2^+$). It is intriguing to note that such an ion can be postulated as an indazole ion radical (CXLIII), an aza analogue of (CXXXIX).



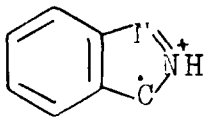
(CXL)



(CXLI)



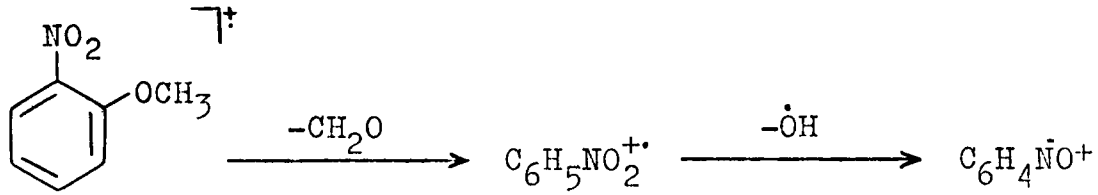
(CXLII)



(CXLIII)

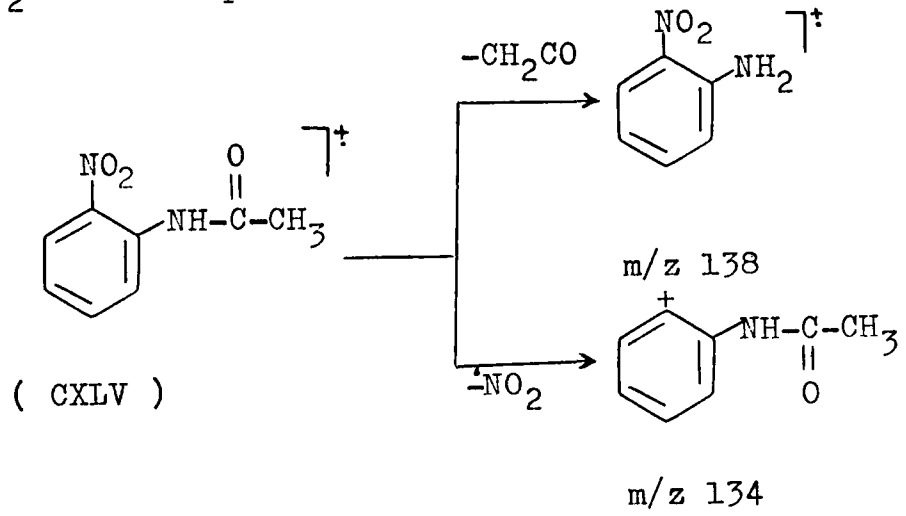
o-Nitroanisole (CXLIV) gives an abundant molecular ion from which there is no significant loss of NO or NO_2. Instead, the elements of formaldehyde are eliminated to afford a peak at m/z 123 ($C_6H_5NO_2^+$) which does not decompose in the same manner as the m/z 123 ion obtained from either o-nitrobenzoic acid (CXXXV) or o-nitroacetophenone (CXXXVIII). It fragments further by elimination of a hydroxyl radical to m/z 106($C_6H_4NO^+$) as substantiated by an appropriate metastable peak. These

observations strongly suggest hydrogen rearrangement to oxygen in this case. The base peak at m/z 77 ($C_6H_5^+$) may arise either by a process involving direct hydrogen migration to aromatic nucleus or by a double hydrogen transfer reaction. The ion at m/z 91 is a doublet whose components ($C_6H_5N^+$, 60%) and ($C_6H_3O^+$, 40%) must be formed by complex processes.



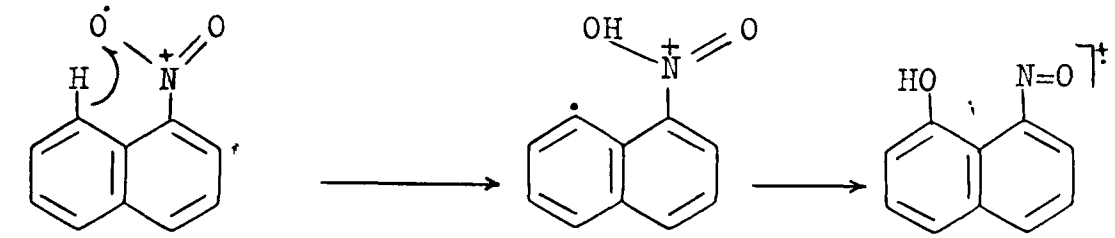
(CXLIV) m/z 123 m/z 106

The mass spectrum of o-nitroacetanilide (CXLV)[91] gives the molecular ion of o-nitroaniline (m/z 138) after the elimination of ketene from the parent ion. This follows from the fact that the spectrum of (CXLV) below the m/z 138 is essentially the same as that of o-nitroaniline (CXXVII) with the exception of a peak at m/z 134 which arises by the loss of NO_2 from the parent ion.

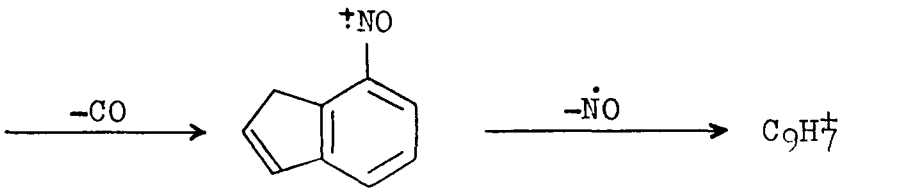


(CXLV) m/z 134

Other aromatic nitro compounds undergo intriguing bond forming reactions upon electron-impact, and though not typical, are certainly of mechanistic interest. A somewhat interesting example comes from the mass spectrum of 1-nitronaphthalene (CXLVI)[91,92] which contained an (M^+-28) ion at m/z 145, shown by high resolution to arise through elimination of CO from the molecular ion. Such (M^+-CO) ions are not observed in the spectra of simple nitrobenzenes. The most reasonable inference is that the peri carbon atom (C-8) is eliminated after the formation of a bond between C-8 and an oxygen atom of the nitro group. It was, therefore, proposed that in the molecular ion of 1-nitronaphthalene (CXLVI) successive hydrogen migration and hydroxyl migration may occur. The resulting nitrosophenol (CXLVII) can then eliminate CO exactly as observed in the mass spectra of phenols[93].

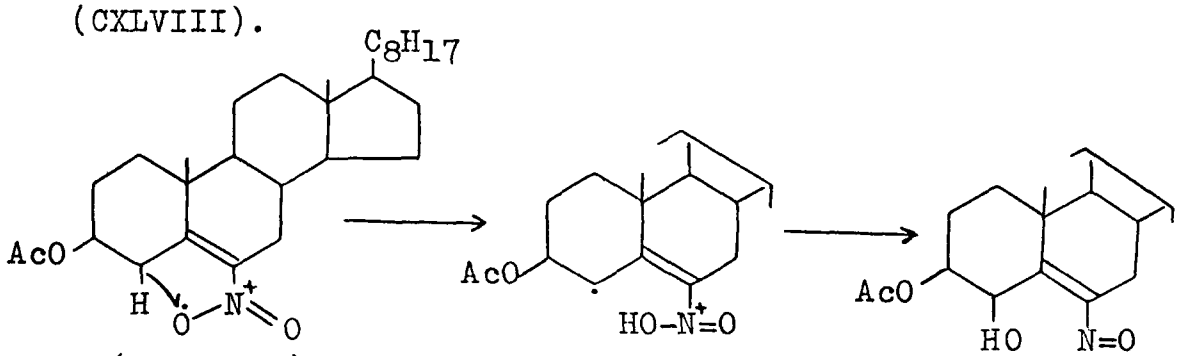


(CXLVI) (CXLVII)



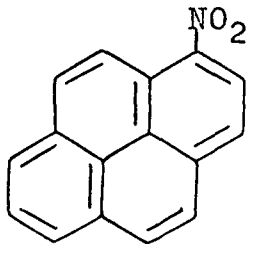
m/z 145 m/z 115

Moreover, the (M^+-CO) ion decomposes by loss of NO to m/z 115 ($C_9H_7^+$) as might be expected on the basis of the proposed mechanism. An excellent photochemical analogy for this postulate is available in the mechanism[94] for oxidation of C_4 on photolysis of 6-nitrocholest-5-en-3β-yl acetate (CXLVIII).

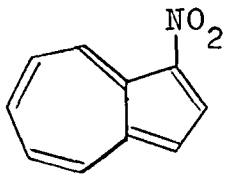


(CXLVIII)

The scope of this unusual CO elimination is fairly limited, as demonstrated[95] by the virtual absence of (M^+-CO) peaks in the mass spectra of 1-nitropyrene (CXLIX) and 1-nitroazulene (CL). Amino- or fluoro-substituents at C-2 of 1-nitronaphthalene(CXLVI) favour the tendency to eject CO, but the same substituents decrease the prevalence of this process when attached to C-6 or C-7[95].



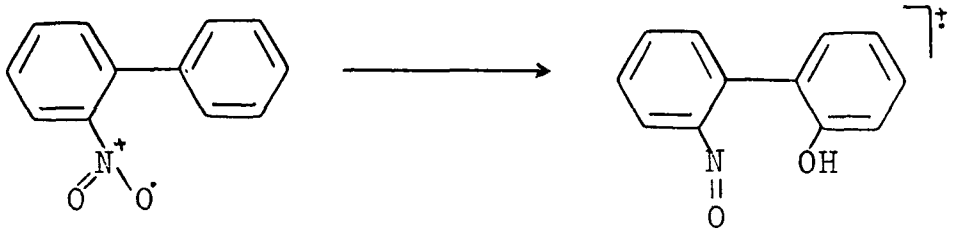
(CXLIX)



(CL)

The mass spectrum of nitrobiphenyl (CLI)[83] shows a number of interesting features that can be rationalized in terms of steric and mesomeric effects.

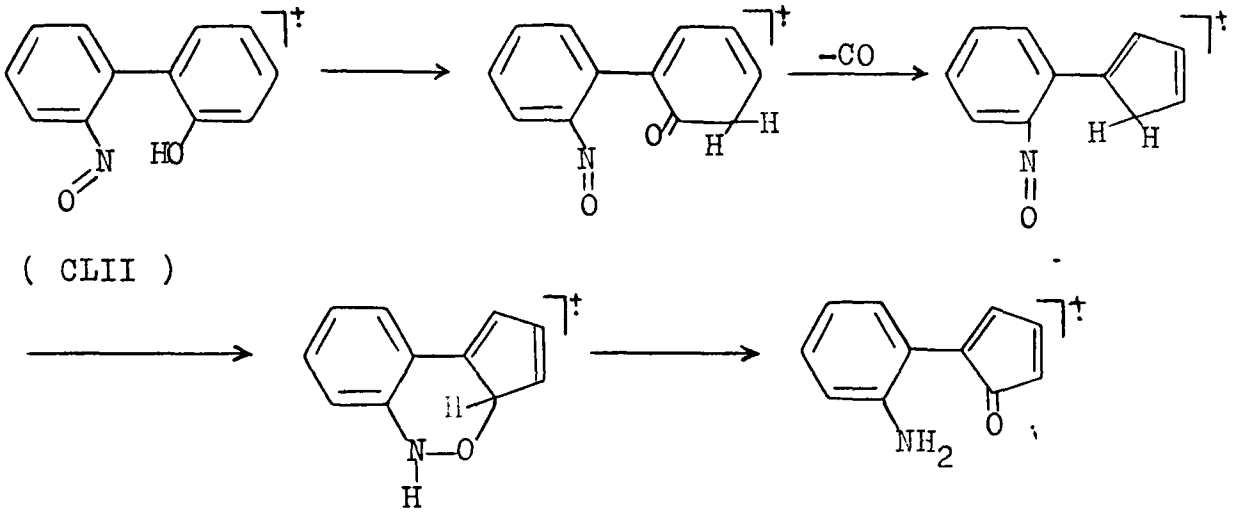
The intensity of the (M^+-17) ion due to the loss of OH is substantial in the spectrum of o-nitrobiphenyl (CLI) even though not as prominent as in o-nitrotoluene (CXXVIII). Evidently, a sterically accessible ring hydrogen atom can participate in this reaction despite being more tightly bonded than a benzylic hydrogen. The comparatively low intensity of the product ion from this reaction may be due in part to the competition from another reaction path unique among the ortho isomers. Among the nitrobiphenyls and not observed in o-nitrotoluene (CXXVIII) is the sequential loss of two molecules of CO. The primary decomposition step in this path suggests isomerization of the parent ion to 2-(2'-nitrosophenyl) phenol (CLII).



(CLI) (CLII)

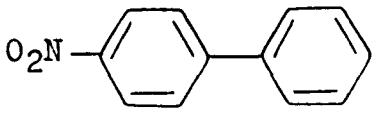
The nitrosophenylphenol structure (CLII), like phenol itself, would be expected to lose CO via a cyclohexadiene intermediate. This decomposition step is evidently accompanied

by the making of new C-O bond as in nitrotoluene.

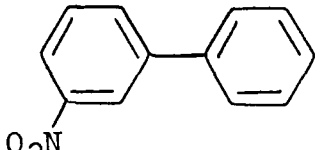


(CLII)

The itensity of (M^+-30) ion, due to the loss of NO is far higher in the spectrum of p-nitrobiphenyl (CLIII) than in that of the meta isomer (CLIV). This pattern resembles that of the corresponding nitropehnols and to a lower extent, the nitroanilines rather than the nitrotoluenes. The expalnation most likely lies in the greater stabilization available to the phenyl phenoxy ion derived from the para isomer, by virtue of interaction with the second phenyl ring, than to that derived on the meta isomer.



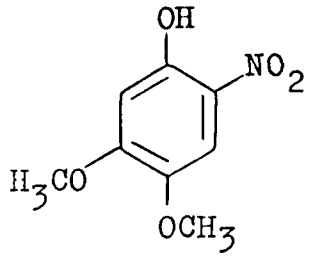
(CLIII)



(CLIV)

The intense peaks at m/z 152 in the spectra of all the three nitrobiphenyls correspond to $C_{12}H_8^+$ which is shown to arise by successive loss of NO_2 and H. Most likely, this is a biphenylene ion, formed directly in breakdown of the ortho isomer and perhaps via a phenylbenzene intermediate in that of the meta and para isomers. Phenylbenzene ions almost certainly do not have localized double and triple bonds, thus the three isomers form biphenylene with about equal ease.

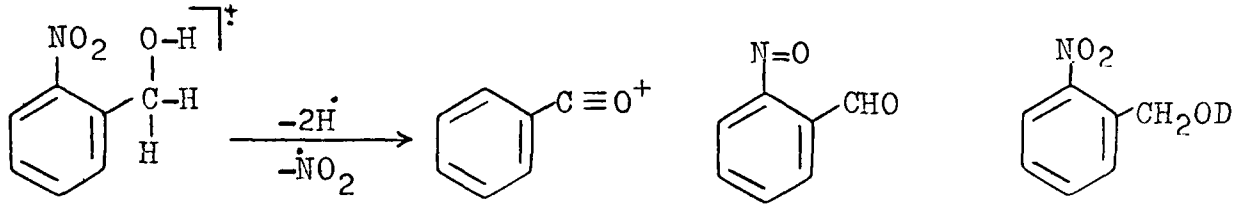
In the spectrum of 4,5-dimethyoxy-2-nitrophenol (CLV), the features characteristic of nitroarenes, and particularly of ortho substituted nitroarenes, do not stand out prominently but are obscured by products of reactions involving the ortho substituents. The most abundant fragment ion arises by the loss of CH_3, suggesting that a methoxy group is a preferred centre of reactivity and presumably of charge localization in the parent ion.



(CLV)

The mass spectrum of o-nitrobenzyl alcohol (CLVI)[91] contains no molecular ion. The highest mass peak is due to an M-3 fragment. The spectrum is remarkable for the presence

of an abundant $M^{+}-H_2O$ (m/z 135, $C_7H_5NO_2^{+}$) ion whereas no loss of a hydroxyl radical occurs. The ($M^{+}-H_2O$) fragment does not retain the label in the spectrum of O-d_1 of o-nitrobenzyl alcohol (CLVII).



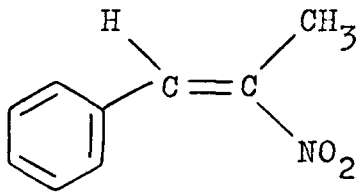
(CLVI) m/z 105 (CLVIII) (CLVII)

It is noteworthy that the photolysis of o-nitrobenzyl alcohol (CLVI) leads to o-nitrosobenzaldehyde (CLVIII) by loss of water[96]. The benzyl ion (m/z 105, $C_7H_5O^{+}$) and the phenyl cation (m/z 77, $C_6H_5^{+}$) are both shifted by one mass unit in the spectrum of deuterated analogue establishing that the hydroxyl proton can replace the nitro group on the aromatic nucleus.

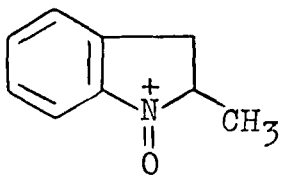
A number of β-nitrostyrenes have been investigated[97] mass spectrometrically and were found to exhibit some of the characteristics of both aromatic and aliphatic nitro compounds. The mass spectrum of β-methyl-β-nitrostyrene (CLIX) may serve for illustrative purposes. The relatively strong molecular ion peak is reminiscent of aromatic nitro compounds as is the loss of nitric oxide (m/z 133). This shows that β-nitrostyrenes but not aliphatic nitro olefins[97], can rearrange to their

isomeric nitrites and it is pertinent to note that photochemical precedent[98] exists for such a reaction. The resemblance to aliphatic nitro compounds is indicated by the elimination of the NO_2 group (m/z 117) together with or followed by the loss of one or two hydrogen atoms. The base peak (m/z 115) at 70 eV corresponds to the loss of the elements of H_2NO_2, but at lower electron voltage the intensity of this peak drops rapidly at the expense of its m/z 116 and m/z 117 neighbours.

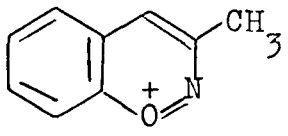
Of considerable interest in the mass spectrum of (CLIX) are the peaks at m/z 146, 135 and 105. The genesis of these peaks has been clarified[97] by deuterium and ^{13}C labelling. The loss of a hydroxyl radical with production of the ion of mass 146 involves one of the ortho ring hydrogens and the resulting species can therefore be formulated[97] either as (CLX) or (CLXI).



(CLIX)



(CLX)



(CLXI)

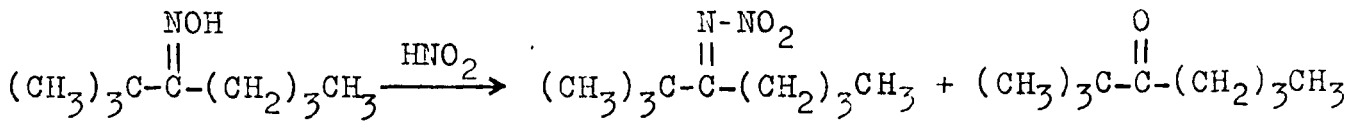
The expulsion of CO from the molecular ion of (CLVIII) gives a fragment ion at m/z 135. The ^{13}C labelling of the nitrostyrene (CLIX) shows that this fragment ion arises by the loss of one of the ring carbon atoms. Similarly, an intense peak at m/z 105 is also observed which corresponds not to the benzoyl cation but rather to a hydrocarbon species resulting from the loss of CO and NO from the molecular ion.

D I S C U S S I O N

PART - ONE

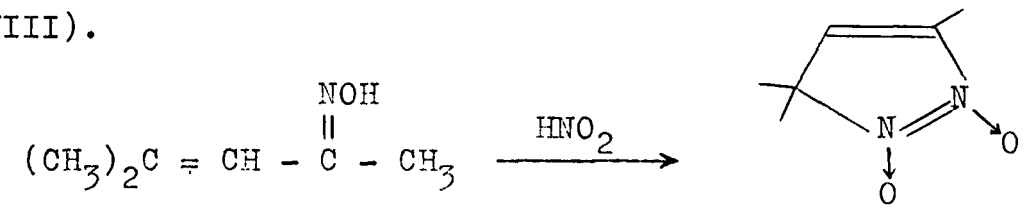
NITROSATION OF STEROIDAL KETOXIMES

Ketoximes have been shown to undergo a less familiar but interesting reaction with nitrosating agents to give a series of compounds. The nature of these compounds depends mainly unpon the structure of the oxime, the nature of the nitrosating agent and the reaction conditions. Saturated ketoximes when treated with nitrous acid at room temperature, give rise to nitrimines. The nitrimine formation is usually accompanied with the deoximation to give a small amount of the parent ketone. 3-Oximino-2,2-dimethylehptane (XXI) for example, gives the nitrimine (XXII) and the parent ketone (XXIII) on treatment with nitrous acid[37].



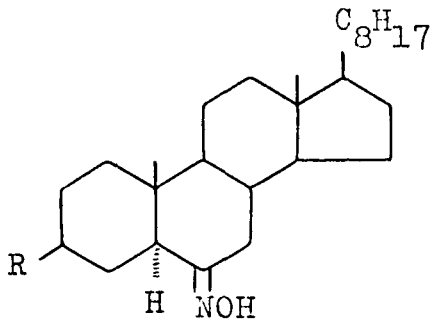
(XXI) (XXII) (XXIII)

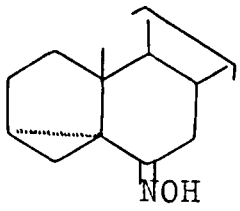
α,β-Unsaturated ketoximes react with nitrous acid to give a series of novel heterocycles. Mesityl oxide oxime (XXXV)[43] reacts with nitrous acid to give pyrazolenine dioxide derivative (XXXVIII).

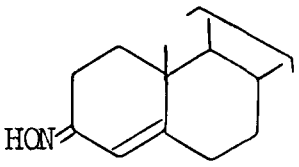


(XXXV) (XXXVIII)

A survey of the literature revealed that no significant application of the nitrosation reaction has been made in the field of steroids. This prompted us to undertake the nitrosation of some easily accessible steroidal ketoximes, both saturated as well as α,β-unsaturated. The ketoximes subjected to nitrosation reaction are 6-oximino-5α-cholestane (CLXII), 6-oximino-5α-cholestan-3β-yl chloride (CLXVII), 6-oximino-5α-cholestan-3β-yl acetate (CLXX), 6-oximino-3α,5-cyclo-5α-cholestane (CLXXII), 3-oximinocholest-4-ene (CLXXV), 7-oximinocholest-5-ene (CLXXXII), 7-oximinocholest-5-en-3β-yl chloride (CLXXXVI), 7-oximinocholest-5-en-3β-yl acetate (CXC) and 3,6-dioximino-5α-cholestane (CXCII).







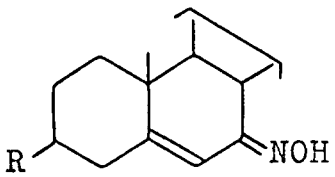
(CLXII) R = H

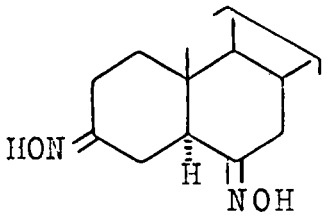
(CLXVII) R = Cl

(CLXX) R = OAc

(CLXXII)

(CLXXV)





(CLXXXII) R = H (CXCII)

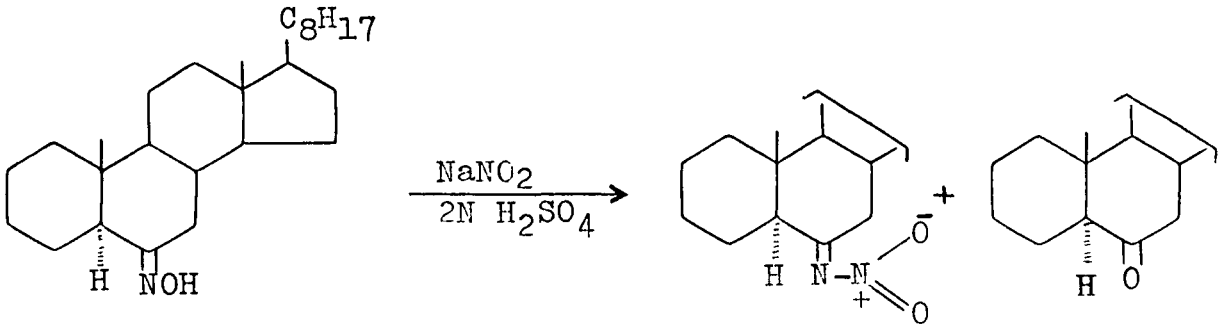
(CLXXXVI) R = Cl

(CXC) R = OAc

Nitrosation of 6-oximino-5α-cholestane (CLXII)

The oxime was prepared according to the literature procedure[99] [$\nu_{max.}$ 3260 (NOH), 1670 cm^{-1} (C=N); δ 9.8 (s, NOH, exchangeable with D_2O), 0.93, 0.83, 0.68 (methyl protons)]. The spectral data for the oxime were obtained for total identification and for comparison purposes.

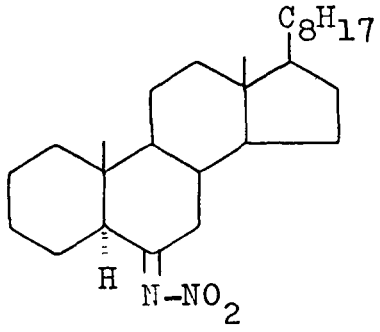
The oxime (CLXII) on treatment with sodium nitrite and 2N sulphuric acid at room temperature afforded, after usual work up and chromatography over silica gel, two compounds having m.pts. 85° and 98°.



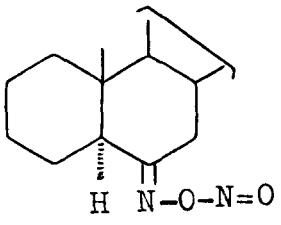
(CLXII) (CLXIII) (CLXIV)

Characterization of the compound m.p. 85° as 6-nitrimino-5α-cholestane (CLXIII)

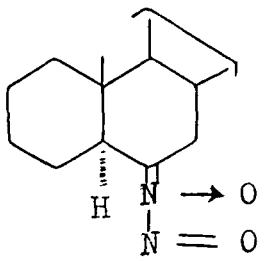
The compound m.p. 85° analysed for $C_{27}H_{46}N_2O_2$. Three possible structures compatible with this analysis are (CLXIII), (CLXV) and (CLXVI).



(CLXIII)



(CLXV)



(CLXVI)

The IR spectrum of the compound m.p. 85° showed strong bands at 1570 and 1320 cm^{-1} and a medium band at 1640 cm^{-1}. The two strong bands at 1570 and 1320 cm^{-1} were ascribed to the unsymmetrical and symmetrical stretching vibrations of the nitro group[31] while the medium band at 1640 cm^{-1} was due to the imine (C=N) stretching frequency of the nitrimine function as in (CLXIII). The structure (CLXV) having an oxime nitrite function can not be accounted for by these spectral values as nitrites exhibit a characteristic doublet in the region 1650-1620 cm^{-1}. Similarly, the structure (CLXVI) having N ⟶ O bond should give a strong band at 1485 cm^{-1}[25].

The NMR spectrum of the compound m.p. 85° showed a signal for two protons at δ 2.7 which was assigned to the C_7-methylene protons. The methyl proton signals were observed at δ 0.95, 0.86 and 0.7.

On the basis of the above mentioned spectral values, the compound m.p. 85° was characterized as 6-nitrimino-5α-cholestane (CLXIII). The acid hydrolysis of the compound to the parent ketone (CLXIV) gave chemical support to the nitrimine structure.

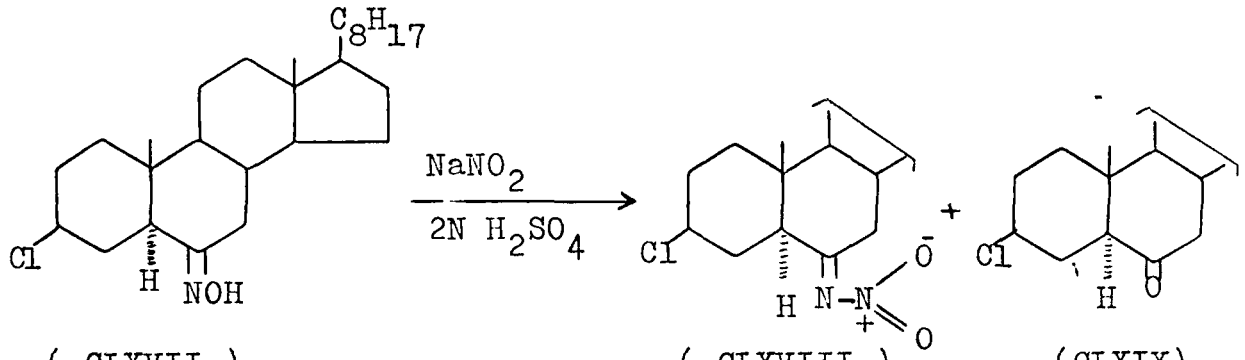
Characterization of the compound m.p. 98° as 6-oxo-5α-cholestane (CLXIV)

The compound m.p. 98° was characterized as 6-oxo-5α-cholestane (CLXIV) on the basis of its spectral data and comparison with the authentic sample[100]. The reported role of nitrous acid as a deoximating agent[5-10] was responsible for the formation of the ketone (CLXIV) from the oxime (CLXII) during nitrosation reaction.

Nitrosation of 6-oximino-5α-cholestan-3β-yl chloride (CLXVII)

The oxime (CLXVII) was prepared according to the procedure described in literature[101] [$\nu_{max.}$ 3280 (NOH), 1665 (C=N), 750 cm^{-1} (C-Cl); δ 9.4 (s, NOH, exchangeable with D_2O), 3.6 (br, $C_3\alpha H$), 0.9, 0.83, 0.7 (methyl protons)].

The oxime (CLXVII) on nitrosation reaction afforded, after usual work up and chromatography over silica gel, two compounds having m.pts. 112° and 128°.



(CLXVII) (CLXVIII) (CLXIX)

Characterization of the compound m.p. 112° as 6-nitrimino-5α-cholestan-3β-yl chloride (CLXVIII)

The compound m.p. 112° analysed for $C_{27}H_{45}N_2O_2Cl$. It gave positive Beilstein test.

The IR spectrum of the compound m.p. 112° showed bands characteristic of 6-nitrimino-5α-cholestan-3β-yl chloride (CLXVIII) [$\nu_{max.}$ 1625 m (C=N), 1570 s (νas NO_2), 1315 s (νs NO_2) and 750 cm^{-1} (C-Cl)]. The NMR spectrum also supported the structure (CLXVIII) for the compound m.p. 112°. A broad multiplet at δ 3.63 ($W_{\frac{1}{2}}$ = 22 Hz) was due to the $C_3\alpha$-H. The methyl proton signals appeared at δ 0.95, 0.83 and 0.7. The nitrimine structure for the compound m.p. 112° was chemically justified by its hydrolysis to the parent ketone (CLXIX) under acidic conditions.

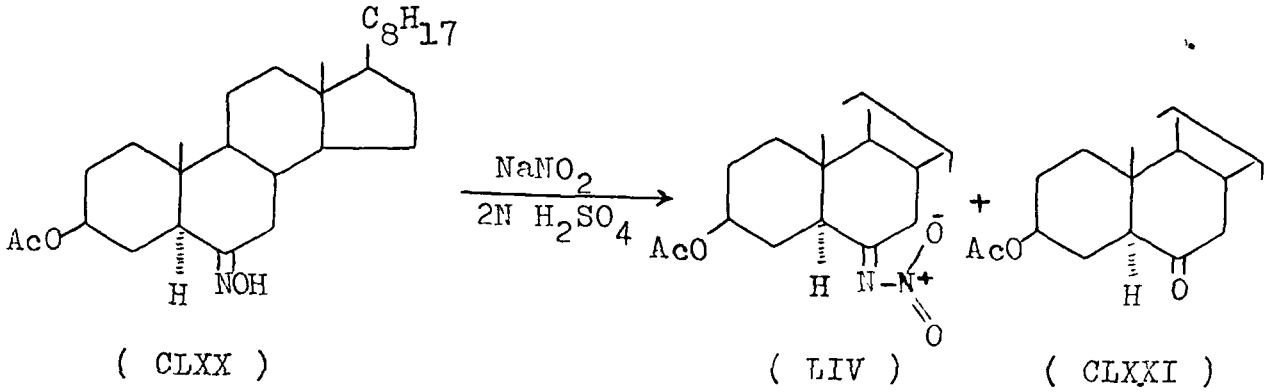
Characterization of the compound m.p. 128° as 6-oxo-5α-cholestan-3β-yl chloride (CLXIX)

The compound m.p. 128° was characterized as 6-oxo-5α-cholestan-3β-yl chloride (CLXIX) on the basis of its spectral properties and comparison with the authentic sample[102]. The ketone formation from the oxime during nitrosation reaction was due to the reported role of nitrous acid as a deoximating agent[5-10].

Nitrosation of 6-oximino-5α-chloestan-3β-yl acetate (CLXX)

6-Oximino-5α-cholestan-3β-yl acetate (CLXX) was prepared according to the literature procedure[103] [$\nu_{max.}$ 3350 (NO-H), 1730 ($CH_3\overset{O}{\overset{\|}{C}}$-O), 1675 (C=N), 1245 cm^{-1} (acetate); δ 8.9 (s, NO$\underline{H}$, exchangeable with D_2O), 4.6 (br, $C_3\alpha$-$\underline{H}$), 1.97 (s, $C\underline{H}_3COO$), 0.93, 0.83, 0.7 (methyl protons)

The oxime (CLXX) on treatment with nitrous acid (prepared in situ by the action of 2N sulphuric acid on sodium nitrite) afforded, after usual work up and chromatography over silica gel, two compounds with m.pts. 135° and 127°.



(CLXX) (LIV) (CLXXI)

Characterization of the compound m.p. 135° as 6-nitrimino-5α-cholestan-3β-yl acetate (LIV)

The compound m.p. 135° analysed for $C_{29}H_{48}N_2O_4$.

The IR spectrum of the compound m.p. 135° showed the characteristic nitrimine bands at 1630 (C=N), 1570 (ν_{as} NO_2) and 1320 cm^{-1} (ν_s NO_2). It also showed bands at 1720 and 1240 cm^{-1} indicating the presence of acetate function. The NMR spectrum of the compound showed a broad multiplet at δ 4.6 ($W_{\frac{1}{2}}$ = 17 Hz) which was assigned to the $C_3\alpha$-H, a sharp singlet for the acetate methyl at δ 1.97 and the methyl protons signals at δ 0.93, 0.83 and 0.7.

On the basis of the above mentioned spectral properties and the formation of the parent ketone (CLXXI) on acid hydrolysis of (LIV), the compound m.p. 135° was characterised as 6-nitrimino-5α-cholestan-3β-yl acetate (LIV).

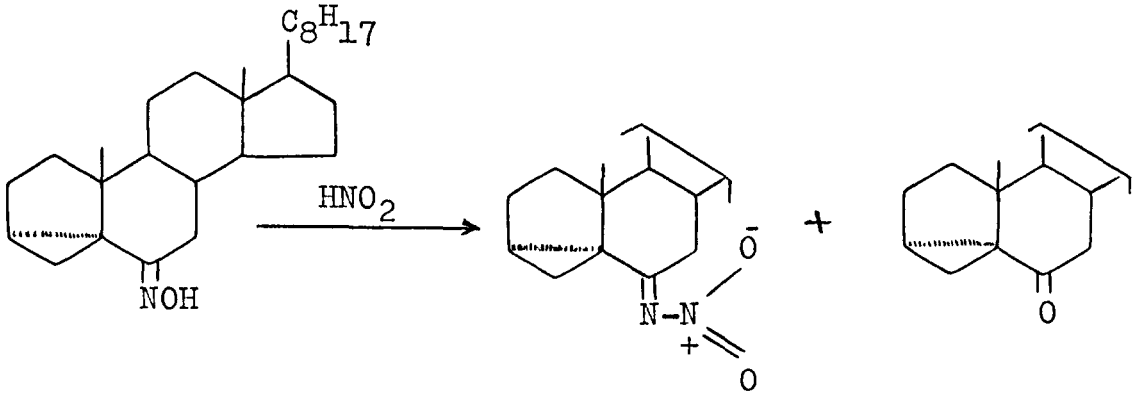
Characterization of the compound m.p. 127° as 6-oxo-5α-cholestan-3β-yl acetate (CLXXI)

The compound m.p. 127° was characterized as 6-oxo-5α-cholestan-3β-yl acetate (CLXXI)[104]. The ketone (CLXXI) was formed during the nitrosation of the oxime (CLXX) due to the nitrosative deoximation[5-10] by nitrous acid.

Nitrosation of 6-oximino-3α,5-cyclo-5α-cholestane (CLXXII)

The oxime was prepared according to the literature procedure[105] [$\nu_{max.}$ 3390 (NOH), 3010 (cyclopropane), 1650 cm^{-1} (C=N), δ 8.8 (br, NO<u>H</u>, exchangeable with D_2O), 0.94, 0.9, 0.83, 0.68 (methyl protons), 0.5-0.6 (complex, cyclopropane protons)].

The oxime (CLXXII) on treatment with nitrous acid underwent N-nitrosation and afforded two compounds with m.pts. 80° and 96°.



(CLXXII) (CLXXIII) (CLXXIV)

Characterization of the compound m.p. 80° as 6-nitrimino-3α, 5-cyclo-5α-cholestane (CLXXIII)

The compound m.p. 80° analysed for $C_{27}H_{44}N_2O_2$. The IR spectrum of the compound showed the characteristic nitrimine bands at 1620 (C=N), 1575 (ν_{as} NO_2) and 1310 (ν_s NO_2) cm^{-1} in addition to a band at 3020 cm^{-1} (cyclopropane).

The NMR spectrum of the compound m.p. 80° showed a complex signal at δ 0.56 for the cyclopropane protons. The methyl protons signals were observed at δ 1.0, 0.93, 0.83 and 0.71.

The nitrimine structure (CLXXIII) for the compound m.p. 80° was chemically supported by its hydrolysis to the parent ketone (CLXXIV) under mild acidic conditions.

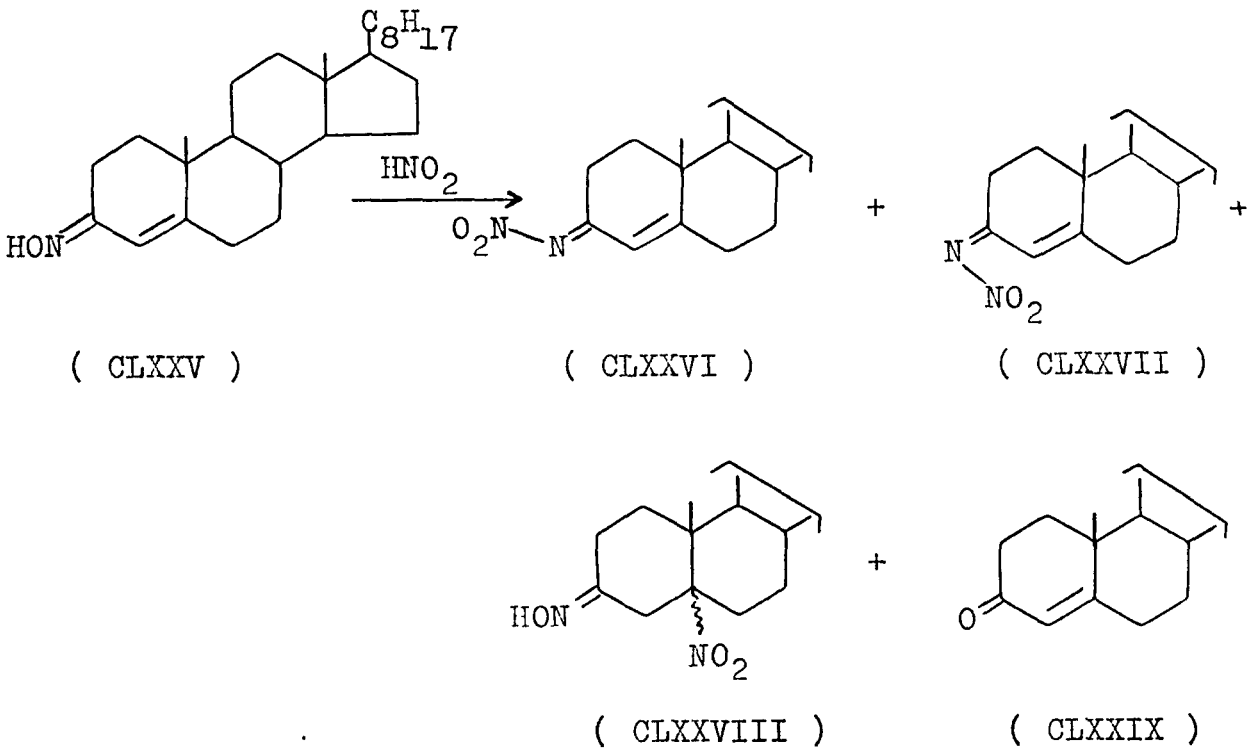
Characterization of the compound m.p. 96° as 6-oxo-3α,5-cyclo-5α-cholestane (CLXXIV)

The compound m.p. 96° was identified to be 6-oxo-3α, 5-cyclo-5α-cholestane (CLXXIV) on the basis of its spectral properties and comparison with the authentic sample[106].

Nitrosation of 3-oximinocholest-4-ene (CLXXV)

3-Oximinocholest-4-ene (CLXXV) was prepared according to the procedure described in literature[107] [$\nu_{max.}$ 3290 (NOH), 1640 (C=N), 1615 cm^{-1} (C=C); δ 7.9 (s, NO<u>H</u>; exchangeable with D_2O), 6.5 (s, C_4-vinylic <u>H</u>), 1.1, 0.9 , 0.8, 0.71 (methyl protons)]. The spectral data for the oxime were obtained for identification and for comparison purposes.

The oxime (CLXXV) on treatment with nitrous acid at room temperature afforded, after usual work up and chromatography over silica gel, four compounds with m.pts. 105°, 142°, 175° and 79°.

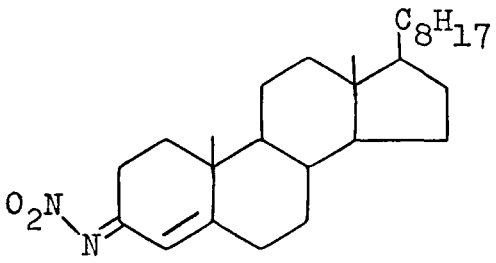


(CLXXV) (CLXXVI) (CLXXVII)

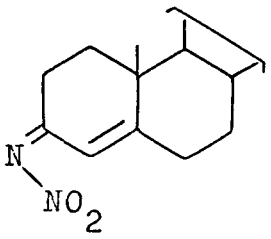
(CLXXVIII) (CLXXIX)

Characterization of the compound m.p. 105° as anti-3-nitrimino-cholest-4-ene (CLXXVI)

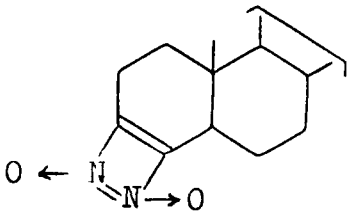
The compound m.p. 105° analysed for $C_{27}H_{44}N_2O_2$. Three possible structres compatible with the elemental analysis are anti- and syn-forms of 3-nitriminocholest-4-ene (CLXXVI) and (CLXXVII) respectively, corresponding to the two isomeric forms of the parent oxime (CLXXV) and a pyrazolenine dioxide type of structure (CLXXX).



(CLXXVI)



(CLXXVII)



(CLXXX)

The IR spectrum of the compound m.p. 105° showed the characteristic nitrimine bands at 1640 (C=N), 1565 (ν_{as} NO_2) and 1320 cm^{-1} (ν_s NO_2). A medium band at 1620 cm^{-1} was indicative of the fact that the carbon-carbon double bond remained intact during the nitrosation reaction. These spectral properties excluded the possibility of the assignment of the pyrazolenine dioxide structure (CLXXX) to the compound m.p.105°.

The distinction between the nitrimine structures (CLXXVI) and (CLXXVII) was possible on the basis of the NMR spectrum. The compound m.p. 105° showed the C_4-vinylic proton signal at δ 5.8 which was analogous to the vinylic proton signal observed in anti-3-oximinocholest-4-ene[108]. It was on the basis of this analogy that the compound m.p. 105° was characterized as anti-3-nitriminocholest-4-ene (CLXXVI). The acid hydrolysis of (CCXXVI) to the parent ketone (CLXXIX) gave chemical support to the nitrimine structure.

Characterization of the compound m.p. 142° as syn-3-nitrimino-cholest-4-ene (CLXXVII)

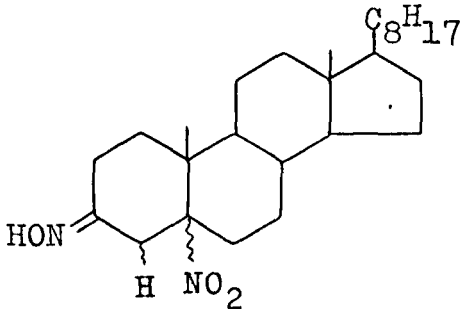
The compound m.p. 142° analysed for $C_{27}H_{44}N_2O_2$, the same as the nitrimine (CLXXVI). The compound was identified to be syn-3-nitriminocholest-4-ene (CLXXVII) on the basis of its IR spectrum which showed the characteristic nitrimine absorption bands at 1660 (C=N), 1560 ($\nu_{as}NO_2$) and 1340 ($\nu_s NO_2$) cm^{-1} and the NMR spectrum which exhibited a downfield shift of the C_4-vinylic proton signal (δ 6.9). The assignment of syn-geometry to the nitrimine (CLXXVI) was by analogy with the syn-form of the parent oxime[108]. The nitrimine (CLXXVII) gave the ketone (CLXXIX) on acid hydrolysis, justifying thereby the nitrimine structure.

Characterization of the compound m.p. 175° as 3-oximino-5α-nitrocholestane (CLXXVIII)

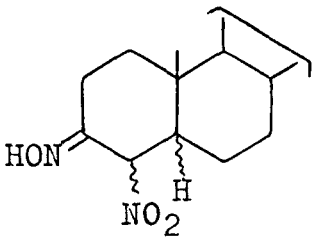
The compound m.p. 175° analysed for $C_{27}H_{46}N_2O_3$. It is evident from the analysis that a molecule of nitrous acid (HNO_2) has been added to the oxime (CLXXV) ($C_{27}H_{45}NO$).

The IR spectrum of the compound m.p. 175° showed absorption bands at 3320, 1630, 1560 and 1350 cm^{-1}. The bands at 3320 (NOH) and 1630 cm^{-1} (C=N) were indicative of the fact that the oxime function has remained unaffected during the course of nitrosation reaction. The two bands at 1560 and 1350 cm^{-1} (characteristic

bands for the nitro group absorption[31]) and the absence of a band for the C=C in IR and vinylic proton signal in NMR spectrum of the compound, suggested that a molecule of nitrous acid has been added across the carbon-carbon double bond. The two possible structures arising from such an addition may be (CLXXVIII) and (CLXXXI).



(CLXXVIII)

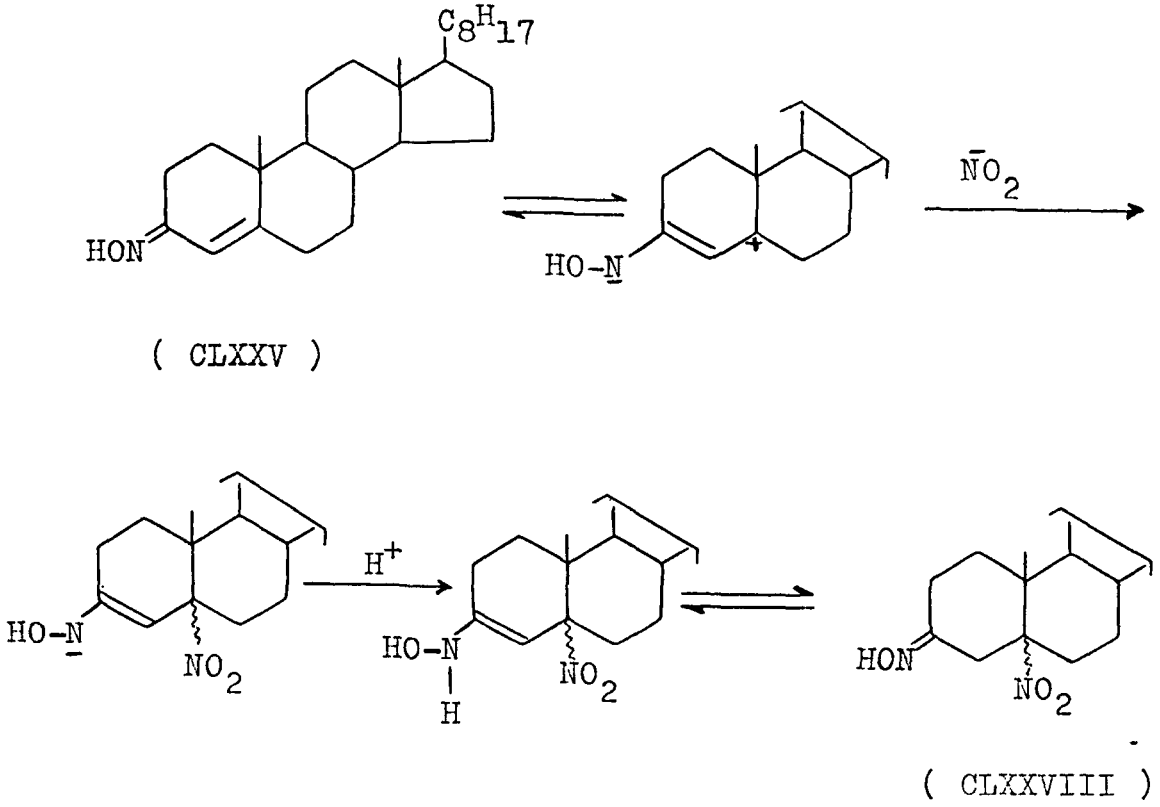


(CLXXXI)

A clear distinction between the structures (CLXXVIII) and (CLXXXI) could be made on the basis of the NMR spectrum. The NMR spectrum of the compound m.p. 175° showed an oxime proton signal at δ 8.6, a broad signal at δ 2.7-2.9 for four protons ($C_2-\underline{H}_2$ and $C_4-\underline{H}_2$) and methyl protons signals at δ 1.1, 0.93, 0.81 and 0.7. These NMR values are best accommodated in structure (CLXXVIII) rather than (CLXXXI) which would give a downfield signal (δ 4.6-4.8) for the C_4H^{109}. The compound m.p. 175° was thus characterized as 3-oximino-5ξ-nitrocholestane (CLXXVIII).

The probable mechanism for the formation of the nitrooxime (CLXXVIII) from (CLXXV) during the nitrosation reaction has been shown in scheme 11.

Scheme - 11



(CLXXV)

(CLXXVIII)

Characterization of the compound m.p. 79° as 3-oxocholest-4-ene (CLXXIX)

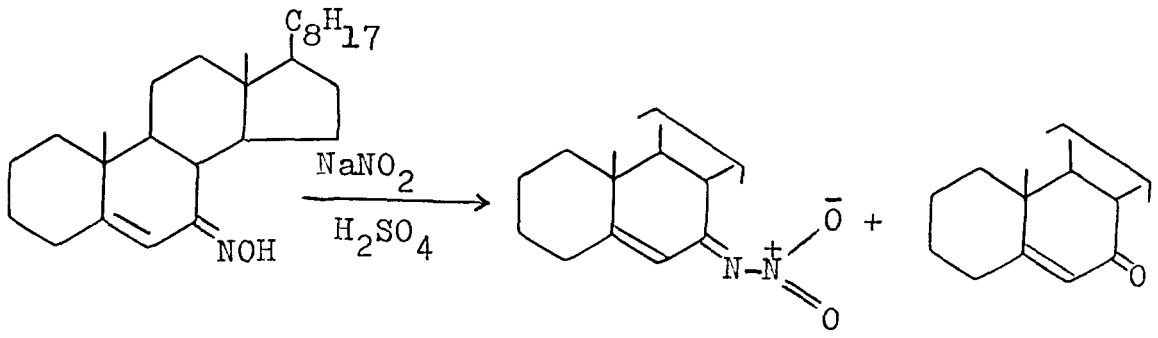
The compound m.p. 79° was characterized as 3-oxocholest-4-ene (CLXXIX) on the basis of its spectral properties and comparison with an authentic sample[110]. The nitrosative

deoximation[5-10] of the oxime (CLXXV) resulted in the formation of the ketone (CLXXIX).

Nitrosation of 7-oximinocholest-5-ene (CLXXXII)

7-Oximinocholest-5-ene (CLXXXII) was prepared according to the literature procedure[111] [$\nu_{max.}$ 3270 (NOH), 1640 (C=N), 1610 cm^{-1} (C=C); δ 8.1 (s, NO<u>H</u>, exchangeable with D_2O), 5.7 (s, C_6-vinylic <u>H</u>), 1.1, 0.93, 0.8, 0.71 (methyl protons)]. The spectral data for the oxime were obtained for its identification and for comparison purposes.

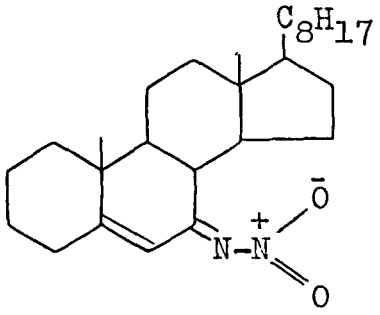
The oxime (CLXXXII) on treatment with nitrous acid at room temperature furnished, after usual work up and chromatography, two compounds with m.pts. 68° and 125°.



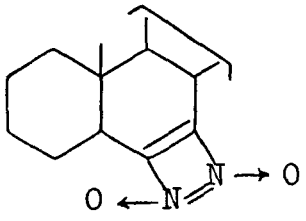
(CLXXXII) (CLXXXIII) (CLXXXIV)

Characterization of the compound m.p. 68° as 7-nitriminocholest-5-ene (CLXXXIII)

The compound m.p. 68° analysed for $C_{27}H_{44}N_2O_2$. Two possible structures compatible with this analysis are the nitrimine (CLXXXIII) and the pyrazolenine dioxide derivative (CLXXXV).



(CLXXXIII)



(CLXXXV)

The IR spectrum of the compound m.p. 68° showed two strong bands at 1565 and 1320 cm^{-1} and two medium bands at 1660 and 1620 cm^{-1}. The strong bands were ascribed to the unsymmetrical and symmetrical stretching vibrations of the nitro group while the medium bands at 1660 and 1620 cm^{-1} were due to (C=N) and (C=C) respectively. These IR values are in accordance with the nitrimine structure (CLXXXIII) and the possibility of the pyrazolenine dioxide type of structure (CLXXXV) is ruled out as it would show a strong band at 1485 cm^{-1}.

The NMR spectrum of the compound m.p. 68° exhibited a vinylic proton signal at δ 5.6 which was assigned to C_6-H. The appearance of the C_6-vinylic proton signal further supported the nitrimine structure (CLXXXIII) as the structure (CLXXXV) lacks a vinylic proton. The methyl protons signals were observed at δ 1.1, 0.91, 0.83 and 0.67.

The chemical support to the nitrimine structure (CLXXXIII) was obtained by its hydrolysis to the parent ketone (CLXXXIV) under acidic conditions.

Characterization of the compound m.p. 125° as 7-oxocholest-5-ene (CLXXXIV)

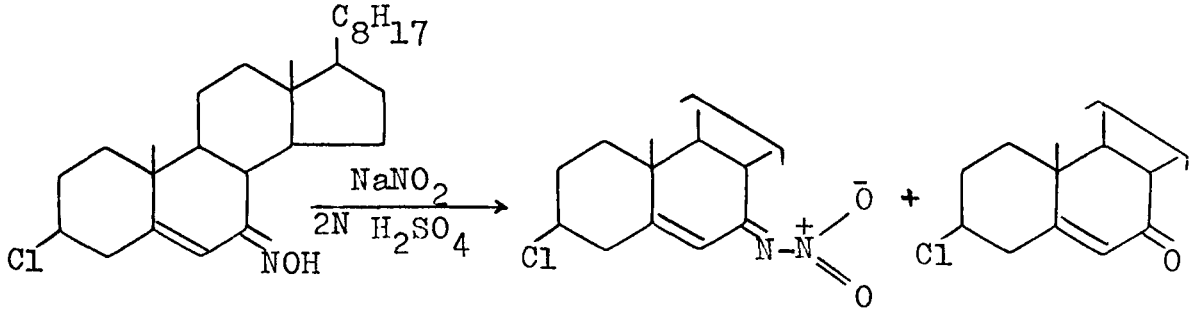
The compound m.p. 125° was characterized as 7-oxocholest-5-ene (CLXXXIV) on the basis of its spectral data and its comparison with an authentic sample[112].

Nitrosation of 7-oximinocholest-5-en-3β-yl chloride (CLXXXVI)

The oxime (CLXXXVI) was prepared according to the literature method[113] [$\nu_{max.}$ 3290 (NOH), 1645 (C=N), 1620 (C=C), 730 cm^{-1} (C-Cl); δ 7.89 (s, NO<u>H</u>, exchangeable with D_2O), 5.76 (s, C_6-vinylic <u>H</u>), 3.55 (m, $C_3\alpha$<u>H</u>), 1.15, 0.91, 0.83, 0.71 (methyl protons)].

The oxime (CLXXXVI) on nitrosation with nitrous acid afforded, after usual work up and column chromatography, two

compounds with m.pts. 138° and 144°.



(CLXXXVI) (CLXXXVII) (CLXXXVIII)

Characterization of the compound m.p. 138° as 7-nitriminocholest-5-en-3β-yl chloride (CLXXXVII)

The compound m.p. 138° analysed for $C_{27}H_{43}N_2O_2Cl$. It gave positive Beilstein test.

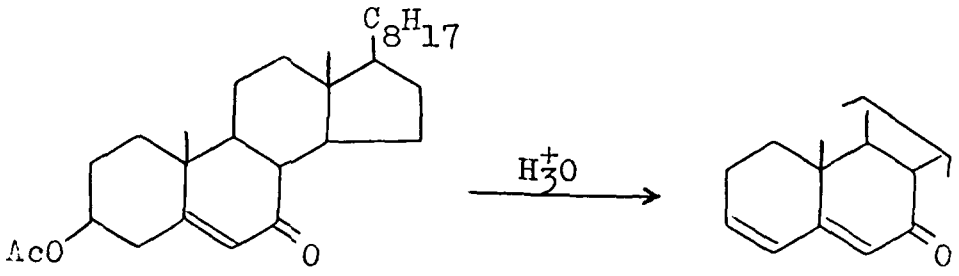
The IR spectrum of the compound m.p. 138° showed the characteristic nitrimine bands at 1640 (C=N), 1565 (ν_{as} NO_2) and 1310 cm^{-1} (ν_s NO_2) besides the two medium bands at 1600 (C=C) and 735 cm^{-1} (C-Cl).

The NMR spectrum exhibited a vinylic proton signal at δ 5.7 which was assigned to C_6H. A multiplet at δ 3.5 ($W_{\frac{1}{2}}$ = 20 Hz) was ascribed to the $C_3\alpha H$. The methyl protons were observed at δ 1.2, 0.9, 0.83 and 0.7.

Thus on the basis of the above spectral properties, the compound m.p. 138° was characterized as 7-nitriminocholest-5-en-3β-yl chloride (CLXXXVII).

The nitrimine structure (CLXXXVII) was chemically justified on the basis of acid catalyzed hydrolysis of the compound m.p. 138° which furnished 7-oxocholesta-3,5-diene (CLXXXIX). The ketone (CLXXXIX) was found to be identical with 7-oxocholesta-3,5-diene prepared according to the literature procedure[114] as shown below (scheme 12).

Scheme - 12



(CXCI) (CLXXXIX)

Characterization of the compound m.p. 144° as 7-oxocholest-5-en-3β-yl chloride (CLXXXVIII)

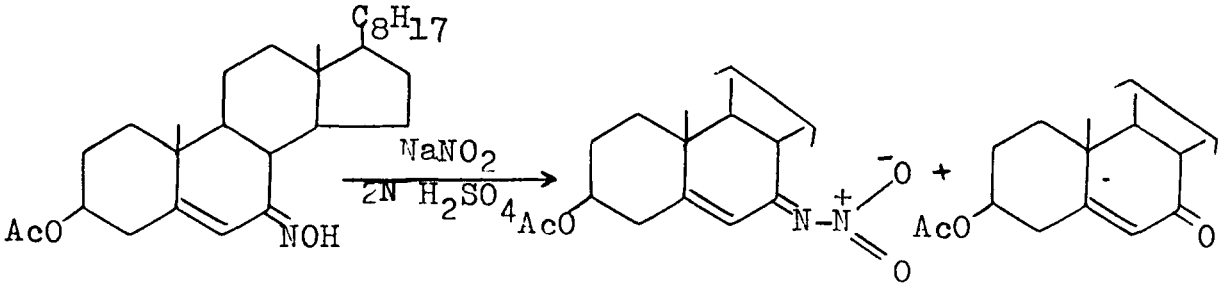
The compound m.p. 144° was characterized as 7-oxocholest-5-en-3β-yl chloride (CLXXXVIII) on the basis of its spectral properties and its comparison with an authentic

sample[115].

Nitrosation of 7-oximinocholest-5-en-3β-yl acetate (CXC)

7-Oximinocholest-5-en-3β-yl acetate (CXC) was prepared according to the procedure described in literature[116] [$\nu_{max.}$ 3450 (NOH), 1735 (CH_3-C(=O)-O), 1630 (C=N), 1600 (C=C), 1275 (acetate), 1040 cm^{-1} (C-O); δ 8.3 (s, NO<u>H</u>, exchangeable with D_2O), 5.68 (s, C_6-vinylic <u>H</u>), 4.5 (m, $C_3\alpha$<u>H</u>), 2.18 (s, CH_3COO), 1.2, 0.93, 0.8, 0.7 (methyl protons)].

The oxime (CXC) on treatment with nitrous acid at room temperature furnished, after usual work up and chromatography over silica gel, two compounds with m.pts. 155° and 162°.



(CXC) (LV) (QXCI)

Characterization of the compound m.p. 155° as 7-nitriminocholest-5-en-3β-yl acetate (LV)

The compound m.p. 155° analysed for $C_{29}H_{46}N_2O_4$. The IR spectrum of the compound showed the characteristic nitrimine

bands at 1640 (C=N), 1570 (ν_{as} NO_2) and 1320 cm^{-1} (ν_s NO_2) in addition to the bands at 1730 (CH_3 $\overset{O}{\overset{\|}{C}}$-O), 1600 (C=C), 1240(acetate) and 1030 cm^{-1} (C-O). The NMR spectrum of the compound m.p. 155° exhibited a vinylic proton signal at δ 5.6 which was ascribed to $C_6\underline{H}$. A broad multiplet at δ 4.6 appeared for the $C_3\alpha H$. The acetate methyl was observed as a singlet at δ 1.97 while the other methyl protons gave signals at δ 1.2, 0.9, 0.81 and 0.73.

On the basis of the above mentioned spectral propterties, the compound m.p. 155° was characterized as 7-nitriminocholest-5-en-3β-yl acetate (LV). The nitrimine structure (LV) for the compound m.p. 155° was chemically justified by the acid catalysed hydrolysis of this compound to 7-oxocholesta-3,5-diene (CLXXXIV)[114]. The ketone was identical with an authentic sample in all respects.

Characterization of the compound m.p. 162° as 7-oxocholest-5-en-3β-yl acetate (CXCI)

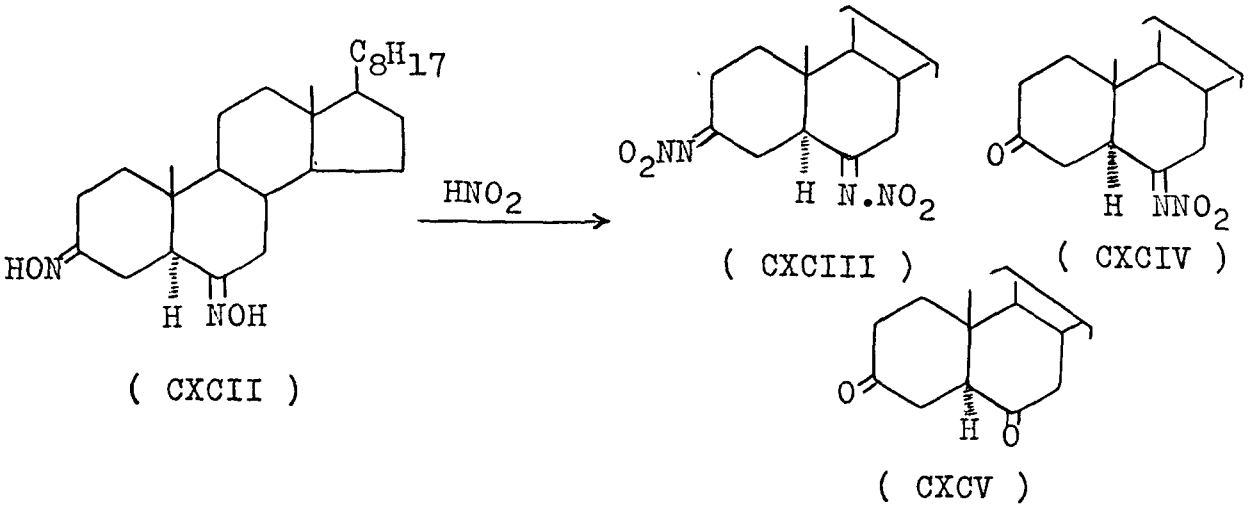
The compound m.p. 162° was identified to be 7-oxocholest-5-en-3β-yl acetate (CXCI) on the basis of its spectral data and comparison with an authentic sample[117].

Nitrosation of 3,6-dioximino-5α-cholestane (CXCII)

The oxime (CXCII) was prepared according to the literature procedure[118] ($\nu_{max.}$ 3320 (NOH), 1640 cm^{-1} (C=N), δ 8.6 (br,

2H, C_3- and C_6-NOH, exchangeable with D_2O), 0.93, 0.8, 0.71, 0.67 (methyl protons).

The oxime (CXCII) on treatment with nitrous acid at room temperature afforded after usual work up and chromatography over silica gel, three compounds having m.pts. 156°, 195° and 167°.



(CXCII) (CXCIII) (CXCIV)

(CXCV)

Characterization of the compound m.p. 156° as 3,6-dinitrimino-5α-cholestane (CXCIII)

The compound m.p. 156° analysed for $C_{27}H_{44}N_4O_4$. It is evident from this analysis that both the oxime groups at C_3 and C_6 have undergone nitrosation.

The IR spectrum of the compound exhibited strong absorptions at 1555-1565 and 1315-1335 cm^{-1} which were characteristic for the unsymmetrical and symmetrical stretching vibrations of the nitro group. The broadness of the two bonds

indicated that there are two nitro groups in the compound. It also showed a medium band at 1640 cm^{-1} for C=N stretching.

The NMR spectrum of the compound was simple, showing signal for $C_5\alpha H$ at δ 2.9. The methyl protons signals were observed at δ 0.93, 0.81, 0.7 and 0.63.

On the basis of these spectral data and the acid hydrolysis of the compound to the parent ketone (CXCV), the compound m.p.156° was characterized as 3,6-dinitrimino-5α-cholestane (CXCIII).

Characterization of the compound m.p. 195° as 6-nitrimino-3-oxo-5α-cholestane (CXCIV)

The compound m.p. 195° analysed for $C_{27}H_{44}N_2O_3$. The IR spectrum of the compound showed a strong carbonyl group absorption at 1715 cm^{-1}, indicating thereby that the diketoxime (CXCII) has undergone deoximation under the reaction conditions to give a carbonyl compound. The spectrum however, also exhibited two strong bands at 1555 and 1340 cm^{-1} which can be ascribed to the unsymmetrical and symmetrical stretching vibrations of the nitro group. A medium band at 1630 was assigned to the imine (C=N) stretching frequency. These bands clearly indicated the presence of a nitrimine function in the compound m.p. 195°. It was therefore concluded that one of the oxime functions of the diketoxime (CXCII) has undergone nitrosation to give nitrimine while the other one has undergone nitrosative deoximation to

form a carbonyl group.

The assignment of the structure (CXCIV) to the compound m.p. 195° was based on the NMR spectrum which exhibited a one proton signal at δ 2.9, assigned to the $C_5\alpha\underline{H}$. It also gave a two proton signal at δ 2.7 (C_7-methylene) and a four protons signal at δ 2.3-2.5 (C_2-and C_4-methylenes).

The acid hydrolysis of the oxonitrimine (CXCIV) furnished 3,6-dioxo-5α-cholestane (CCXV).

Characterization of the compound m.p. 167° as 3,6-dioxo-5α-cholestane (CCXV)

The compound m.p. 167° was characterized as 3,6-dioxo-5α-cholestane (CXCV) on the basis of its spectral properties and by comparison with an authentic sample of the diketone[118].

Table

Spectral Properties of Oximes and Nitrimines

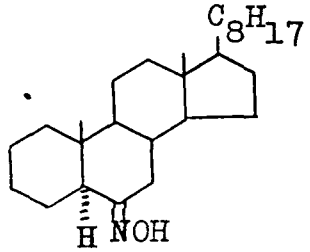
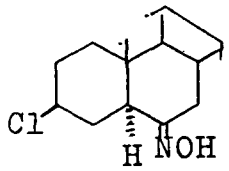
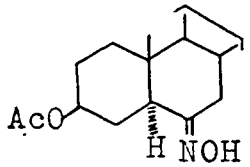
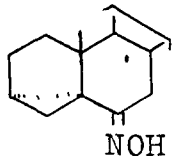
Compound	IR (cm^{-1})	NMR (δ)
 (CLXII)	3260m (NOH), 1670m (C=N).	9.8s (NO<u>H</u>), 0.93, 0.83, 0.68 (methyl protons).
 (CLXVII)	3280m (NOH), 1665m (C=N), 750m (C-Cl).	9.4s (NO<u>H</u>), 3.6br ($C_3\alpha\underline{H}$, $W\frac{1}{2}$ = 17 Hz), 0.9, 0.83, 0.7 (methyl protons).
 (CLXX)	3350m (NOH), 1730s (CH_3COO), 1675m (C=N), 1245s (acetate).	8.9s (NO<u>H</u>), 4.6br ($C_3\alpha\underline{H}$, $W\frac{1}{2}$ = 16 Hz), 1.97s ($C\underline{H}_3COO$), 0.93, 0.83, 0.7 (methyl protons).
 (CLXXII)	3390m (NOH), 3010w (cyclopropane), 1650m (C=N).	8.8s (NO<u>H</u>), 0.94, 0.83, 0.68 (methyl (protons), 0.5-0.6br (cyclopropane protons).

Table contd.

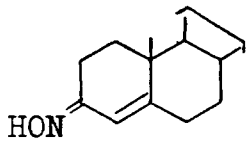
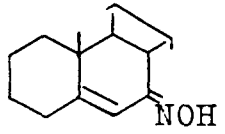
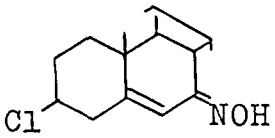
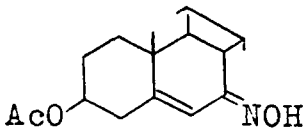
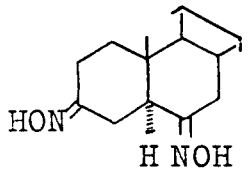
Compound	IR (cm^{-1})	NMR (δ)
 (CLXXV)	3290m (NOH), 1640m (C=N), 1615w (C=C).	7.9s (NO$\underline{H}$), 6.5s (C_4-vinylic $\underline{H}$), 1.1, 0.9 , 0.8, 0.71 (methyl protons).
 (CLXXXII)	3270m (NOH), 1640m (C=N), 1610m (C=C).	8.1s (NO$\underline{H}$), 5.7s (C_6-vinylic $\underline{H}$), 1.1, 0.93, 0.8, 0.71 (methyl protons).
 (CLXXXVI)	3290m (NOH), 1645m (C=N), 1620m (C=C), 730m (C-Cl).	7.89s (NO$\underline{H}$), 5.76s (C_5-vinylic $\underline{H}$), 3.55m ($C_3\alpha\underline{H}$, $W\frac{1}{2}$ = 17 Hz), 1.15, 0.91, 0.83, 0.71 (methyl protons).
 (CXC)	3450m (NOH), 1735s (CH_3COO), 1630m (C=N), 1600m (C=C), 1275s (acetate), 1040m (C-O).	8.3s (NO$\underline{H}$), 5.68s (C_6-vinylic $\underline{H}$), 4.5m ($C_3\alpha\underline{H}$, $W\frac{1}{2}$ = 17 Hz), 2.18s ($C\underline{H}_3COO$ 1.2, 0.93, 0.8, 0.7 (methyl protons).
 (CXCII)	3320m (NOH), 1640m (C=N).	8.6br (2H, $C_3NO\underline{H}$ and $C_6NO\underline{H}$), 0.93, 0.8, 0.71, 0.67 (methyl protons).

Table contd.

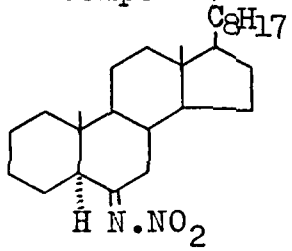
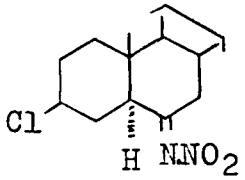
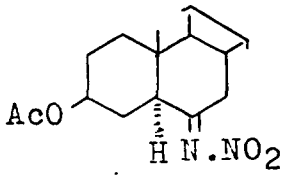
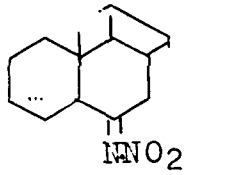
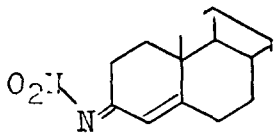
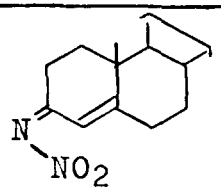
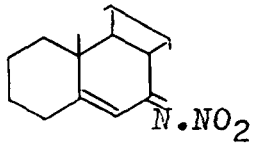
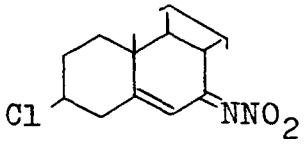
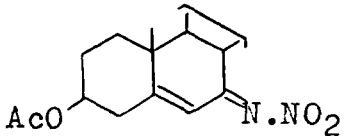
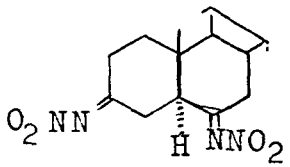
Compound	IR (cm^{-1})	NMR (δ)
 (CLXIII)	1640m (C=N), 1570s ($\nu_{as}NO_2$), 1320s ($\nu_{s}NO_2$).	0.95, 0.86, 0.7 (methyl protons).
 (CLXVIII)	1625m (C=N), 1570s ($\nu_{as}NO_2$), 1315s ($\nu_{s}NO_2$), 750 m (C-Cl).	3.63 m ($C_3\alpha\underline{H}$, $W\frac{1}{2}$ =22 Hz), 0.95, 0.83, 0.7 (methyl protons).
 (LIV)	1720s ($CH_3\overset{O}{\overset{\|}{C}}-O$), 1630m (C=N), 1570s ($\nu_{as}NO_2$), 1320s ($\nu_{s}NO_2$), 1240s (acetate).	4.6 m ($C_3\alpha\underline{H}$, $W\frac{1}{2}$ =17 Hz), 1.97s ($C\underline{H}_3COO$), 0.93, 0.83, 0.7 (methyl protons).
 (CLXXIII)	3020w (cyclopropane), 1620m (C=N), 1575s ($\nu_{as}NO_2$), 1310s ($\nu_{s}NO_2$).	1.0, 0.93, 0.83, 0.71 (methyl protons), 0.56br (cyclopropane protons)
 (CLXXVI)	1640m (C=N), 1620 m (C=C), 1565s ($\nu_{as}NO_2$), 1320s ($\nu_{s}NO_2$).	5.8s (C_4-vinylic $\underline{H}$), 1.1, 0.9, 0.8, 0.67 (methyl protons).

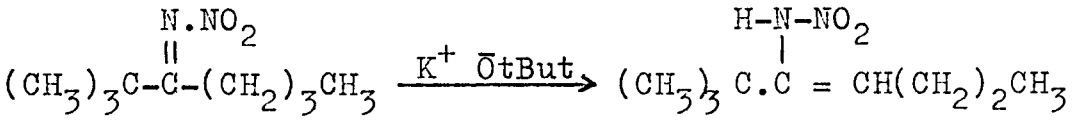
Table contd.

Compound	IR (cm^{-1})	NMR (δ)
 (CLXXVII)	1660m (C=N), 1620 m(C=C), 1560s ($\nu_{as}NO_2$), 1340s ($\nu_{s}NO_2$).	6.9s (C_4-vinylic H), 1.03, 0.9, 0.83, 0.67(methyl protons).
 (CLXXXIII)	1660m (C=N), 1620m (C=C), 1565s ($\nu_{as}NO_2$), 1320s ($\nu_{s}NO_2$).	5.6s (C_6-vinylic H), 1.1, 0.91, 0.83, 0.67 (methyl protons).
 (CLXXXVII)	1640m (C=N), 1600m (C=C), 1565s ($\nu_{as}NO_2$), 1310s ($\nu_{s}NO_2$), 735m (C-Cl).	5.7s (C_6-vinylic H), 3.5m ($C_3\alpha$H, $W\frac{1}{2}$ = 20 Hz), 1.2, 0.9, 0.83, 0.7 (methyl protons).
 (LV)	1730s (CH_3-C(=O)-O), 1640m (C=N), 1600 m (C=C), 1570s ($\nu_{as}NO_2$), 1320s ($\nu_{s}NO_2$), 1240m (acetate), 1030m (C-O).	5.6s (C_6-vinylic H), 4.6m ($C_3\alpha$H, $W\frac{1}{2}$ = 18 Hz), 1.97s (CH_3COO), 1.2, 0.9, 0.81, 0.73 (methyl protons).
 (CXCIII)	1640m (C=N), 1565-1555s ($\nu_{as}NO_2$), 1335-1315s ($\nu_{s}NO_2$).	2.9m ($C_5\alpha$-H), 0.93, 0.81, 0.7, 0.63 (methyl protons).

PART - TWO

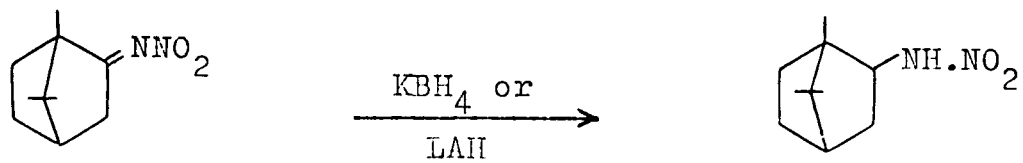
TRANSFORMATIONS OF STEROIDAL NITRIMINES

The nitrimines, prepared by the nitrosation reaction of ketoximes, undergo a series of transformations to give a variety of products. The isomerization of nitrimines with methanolic alkali[58] results in the formation of their less stable isomers called N-nitroenamines. 3-Nitrimino-2,2-dimethylheptane (XXII) for example, changes to the vinylnitramine on treatment with potassium tertiary butoxide[38].



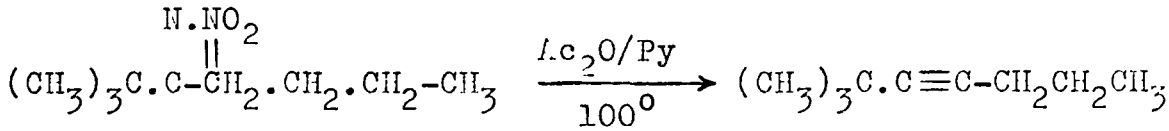
(XXII) (LXIII)

The reduction of nitrimines with complex metal hydrides results in the saturation of the imine (C=N) function and gives rise to N-nitroamines. Camphornitrimine (XVI) changes to bornylamine (LXXI) on treatment with potassium borohydride in ethanol or with lithium aluminium hydride[22].



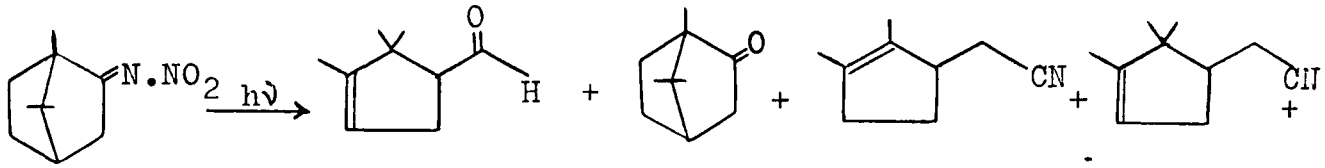
(XVI) (LXXI)

When treated with a mixture of acetic anhydride and pyridine, nitrimines get transformed to acetylenes and/or allenes, depending upon the structure of the nitrimine and the mode of dehydration[38]. The nitrimine (XXII) for example, reacts with acetic anhydride and pyridine at 100°C to give the acetylene (LXXXIV).

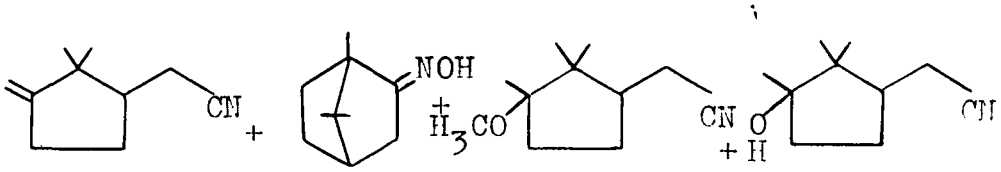


(XXII) (LXXXIV)

The most interesting transformation that the nitrimines undergo, are the thermolytic and photolytic transformations. Photolysis of camphornitrimine (XVI) in methanol resulted in the formation of eight different products (XCV-CII)[66,67].

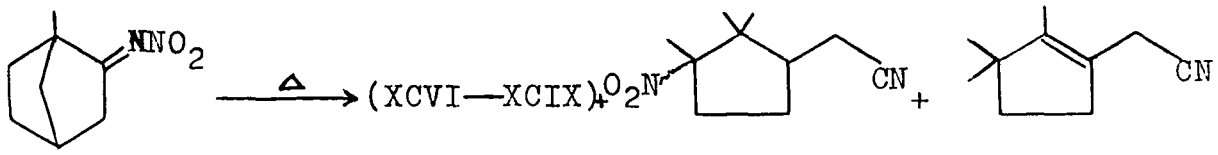


(XVI) (XCV) (XCVI) (XCVII) (XCVIII)



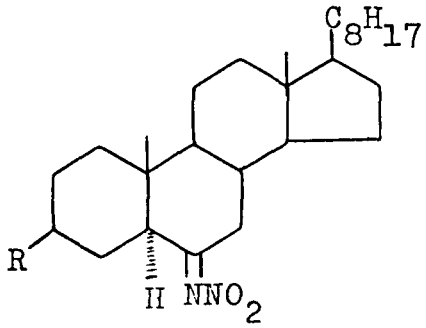
(XCIX) (C) (CI) (CII)

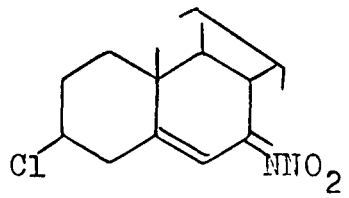
Similarly, thermolysis[67] of (XVI) results in the formation of six different products (XCVI-XCIX, CIII, CIV).



(XVI) (CIII) (CIV)

Motivated by these interesting results of the nitrimine transformations, we carried out the transformations of the steroidal nitrimines. The nitrimines selected for the present study are 6-nitrimino-5α-cholestane (CLXIII), its 3β-chloro-(CLXVIII) and 3β-acetoxy-(LIV) analogues and 7-nitriminocholest-5-en-3β-yl chloride (CLXXXVII).





(CLXIII) R = H

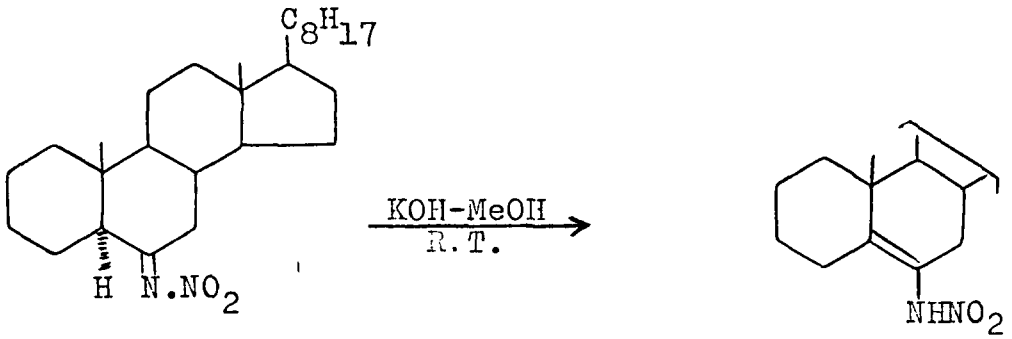
(CLXVIII) R = Cl

(LIV) R = OAc

(CLXXXVII)

Isomerization of 6-nitrimino-5α-cholestane (CLXIII)

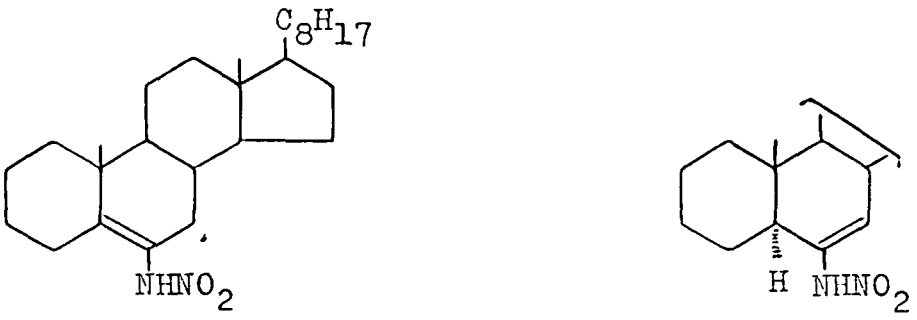
The isomerization of nitrimine (CLXIII) with methanolic potassium hydroxide at room temperature afforded, after usual work up and chromatography over silica gel, a single compound having m.p. 130°



(CLXIII) (CXCVI)

Characterization of the compound m.p. 130° as 6-nitroaminocholest-5-ene (CXCVI)

Being an isomer of (CLXIII) the compound m.p. 130° analysed for $C_{27}H_{46}N_2O_2$. Two possible isomeric nitroenamines, compatible with this analysis are (CXCVI) and (CXCVII).



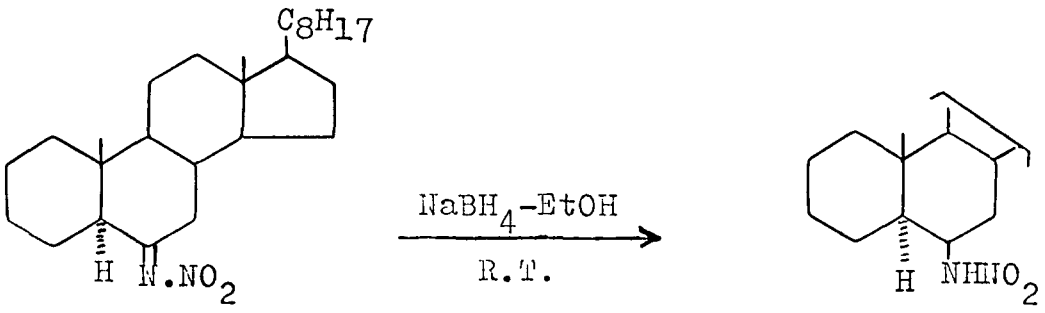
(CXCVI) (CXCVII)

The IR spectrum of the compound m.p. 130° exhibited band at 3320 cm^{-1} which was assigned to the N-H stretching frequency of the amino group. The strong bands at 1535 and 1320 cm^{-1} were due to the unsymmetrical and symmetrical stretching vibrations of the nitro group. The compound also showed a weak band at 1620 cm^{-1} for the carbon-carbon double bond. These IR values were in full agreement with both the probable structures (CXCVI) and (CXCVII).

The assignment of correct structure to the compound m.p. 130° was aided by the NMR spectrum which showed a broad signal at δ 8.5 for the amino proton. The spectrum was however, devoid of any vinylic proton signal, ruling out thereby the possibility of the structure (CXCVII). The compound m.p. 130° was thus characterized as 6-nitroaminocholest-5-ene (CXCVI).

Reduction of 6-nitrimino-5α-cholestane (CLXIII)

The nitrimine (CLXIII) on treatment with sodium borohydride in absolute ethanol at room temperature, furnished after usual work up and column chromatography over silica gel, a non-crystallizable oil.



(CLXIII) (CXCVIII)

Characterization of the oil as 6β-nitroamino-5α-cholestane (CXCVIII)

The compound obtained as a non-crystallizable oil from the reduction of 6-nitrimino-5α-cholestane (CLXIII) analysed for $C_{27}H_{48}N_2O_2$.

The IR spectrum of the compound showed absroption band due to the N-H stretching at 3300 cm^{-1}. The two strong bands at 1535 and 1330 cm^{-1} were due to the unsymmetrical and symmetrical stretching vibrations of the nitro group of the nitroamine (CXCVIII).

The NMR spectrum of the compound showed a doublet at δ 8.75 (J = 6 Hz) which was assigned to the amine proton. A broad multiplet at δ 4.21 ($W_{\frac{1}{2}}$ = 8 Hz)[56] was due to the C_6α-H (equatorial). The half-band width of the signal for C_6-H was indicative of the fact that the configuration of the nitroamine function at C_6 was axial (β-oriented). The methyl protons were observed at δ 0.93, 0.81, 0.7 and 0.68.

Reaction of the nitroamine (CXCVIII) with acetic anhydride-pyridine

In an attempt to prepare N^1-acetyl derivative (CXCIX), the nitroamine (CXCVIII) was treated with acetic anhydride-pyridine at room temperature for 30 minutes. Usual work up of

the reaction mixture afforded an oil (TLC homogeneous). It analysed for $C_{29}H_{50}N_2O_3$ and gave in its IR spectrum significant bands at 1740 s, 1572 w, 1240 s, 1140 m and 1030 s cm^{-1}. The NMR spectrum of the product gave signals at δ 4.3 m($W_{\frac{1}{2}}$=8 Hz; $C_6\alpha$-H), 2.15s(CH_3COO), 0.91, 0.83, 0.71 and 0.68 (other methyl signals).

The strong bands in IR for a nitro group (1570-1550 and 1340-1320 cm^{-1}) were conspicuous by their absence. Instead an acetyloxy group (CH_3COO) was strongly suggested (1740; CH_3COO, 1240, 1140, 1030 cm^{-1}; acetate). The weak band at 1572 cm^{-1} suggested the presence of $-N=\overset{+}{N}-O^-$ moiety[119,120]. As expected the N-H signal in NMR was not observed.

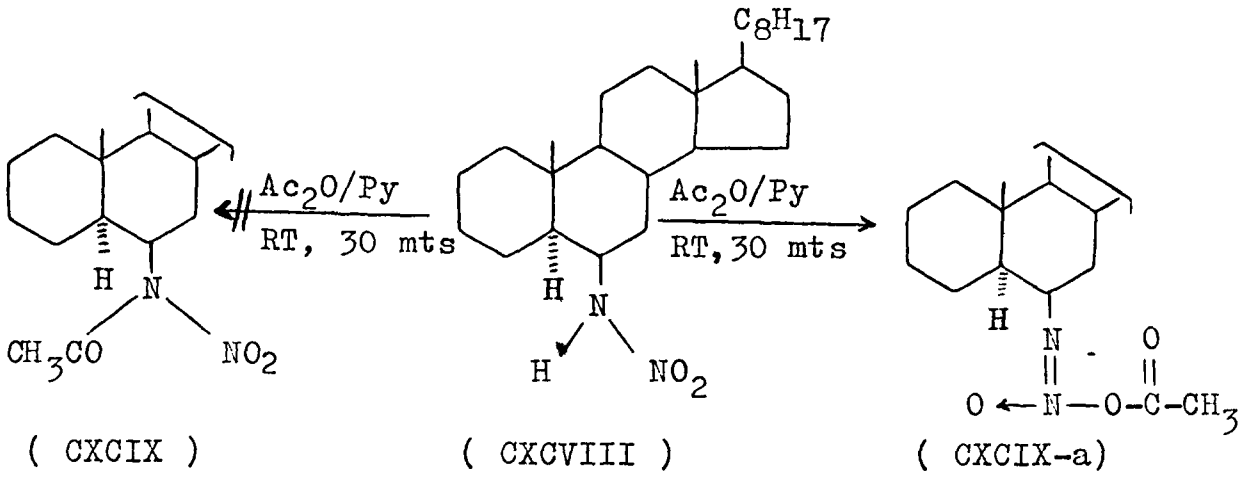
Suarez,et al.[56] in their study on denitroamination of steroidal nitroamines with acetic anhydride-pyridine (room temperature, overnight) suggested that the reaction proceeds via N-oxido intermediate, though they did not report the isolation and characterization of such an intermediate.

$$R\text{-}NH\text{-}NO_2 \rightleftharpoons R\text{-}N=N\text{-}OR' \longrightarrow [R^+ N_2O \bar{O}R'] \longrightarrow \text{products}$$

(N-Oxido Intermediate, R'= CO-alkyl)

From the above precedence it is possible to suggest N-oxidoacetate structure (CXCIX-a) for the product. The spectral values are in better agreement with the structure (CXCIX-a) rather

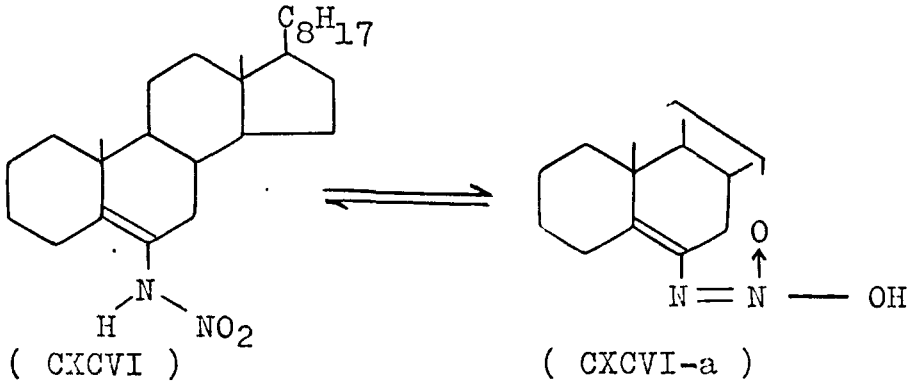
than with (CXCIX).



(CXCIX) (CXCVIII) (CXCIX-a)

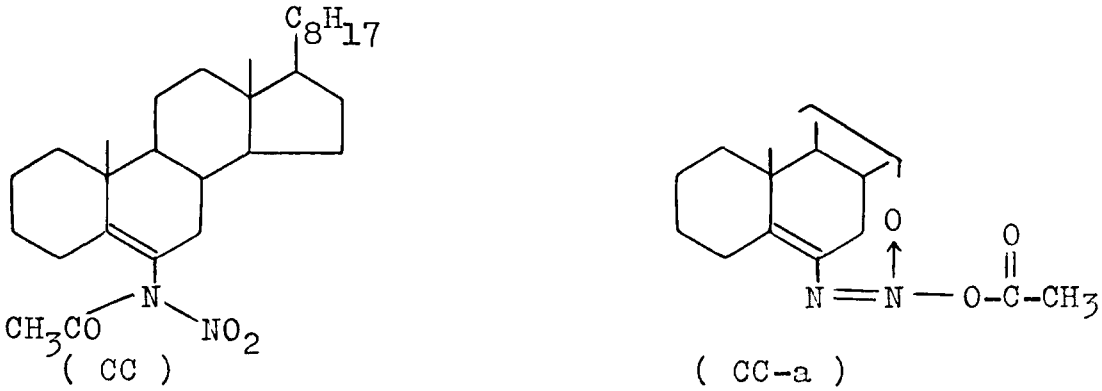
Though we have not conducted the denitroamination from (CXCIX-a), it is reasonable to believe that the N-oxidoacetate structure such as (CXCIX-a) could well be involved as an intermediate as suggested by Suarez, et al.[56]

The above observation promted us to subject the nitroenamine (CXCVI) to acetic anhydride-pyridine reaction. The enamine (CXCVI) possesses part structure $-NH-NO_2$ which is also present in the nitroamine (CXCIX) and therefore capable of equilibrating with the aci-nitroamine structure (CXCVI-a).



(CXCVI) (CXCVI-a)

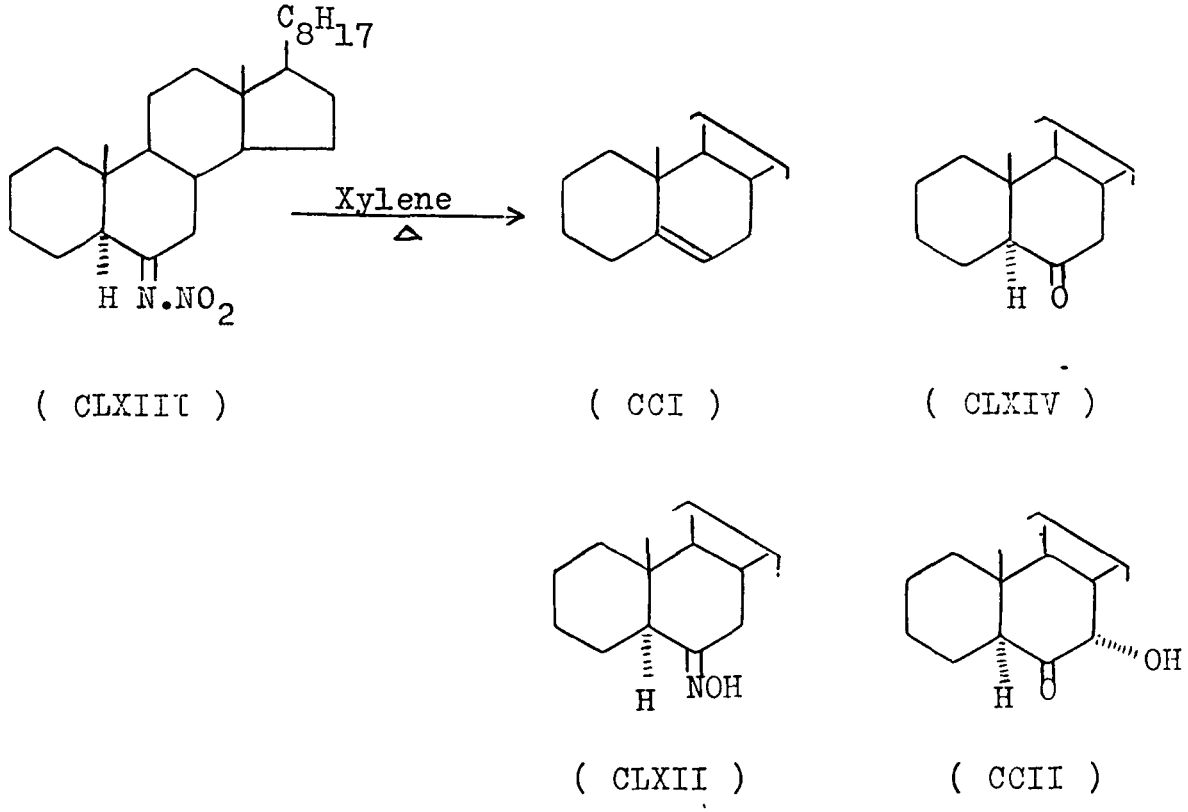
It was therefore, expected that (CXCVI) with acetic anhydride-pyridine should give O-acetyl derivative (CC-a). The reaction of (CXCVI) with acetic anhydride-pyridine gave, after usual work up, a compound which analysed for $C_{29}H_{48}N_2O_3$. The IR spectrum of the compound gave important bands at 1738s, 1570 w, 1245 s, 1030 cm^{-1}. The NMR spectrum gave a singlet for 3 protons at δ 2.06 (CH_3COO). The absence of strong bands (IR) for a nitro group discarded the N-acetyl structure (CC) for the product. By precedence and on the basis of spectral data structure (CC-a) is more acceptable than (CC).



(CC) (CC-a)

Thermolysis of 6-nitrimino-5α-cholestane (CLXIII)

The thermolysis of nitrimine (CLXIII) under refluxing xylene for five hours afforded after the removal of the solvent in vacuo, a brownish oil which on column chromatography gave four compounds having m.pts. 95°, 98°, 200° and 185°.



(CLXIII) (CCI) (CLXIV)

(CLXII) (CCII)

Characterization of the compound m.p. 95° as cholest-5-ene(CCI)

The compound m.p. 95° was identified as cholest-5-ene (CCI) on the basis of its spectral properties [$\nu_{max.}$ 1600 m (C=C) cm^{-1}; δ 5.6 m (C_6-vinylic H), 1.1, 0.91, 0.83 and 0.7 (methyl protons)] and by comparison with an authentic sample,

prepared according to the literature procedure[121].

Characterization of the compound m.p. 98° as 6-oxo-5α-cholestane (CLXIV)

The compound m.p. 98° was characterized as 6-oxo-5α-cholestane (CLXIV) on the basis of its spectral data [$\nu_{max.}$ 1705 s (C=O) cm^{-1}; δ 0.91, 0.83, 0.7 and 0.63 (methyl protons)] and by comparison with an authentic sample of the ketone, prepared according to the literature method[100].

Characterization of the compound m.p. 200° as 6-oximino-5α-cholestane (CLXII)

The compound m.p. 200° was identified as 6-oximino-5α-cholestane (CLXII) on the basis of its spectral values [$\nu_{max.}$ 3260 m(NOH), 1670 m(C=N) cm^{-1}; δ 9.8 s(NO<u>H</u>, exchangeable with D_2O) 0.93, 0.83 and 0.68 (methyl protons)] and by comparison with an authentic sample of the oxime[99].

Characterization of the compound m.p. 185° as 6-oxo-7α-hydroxy-5α-cholestane (CCII)

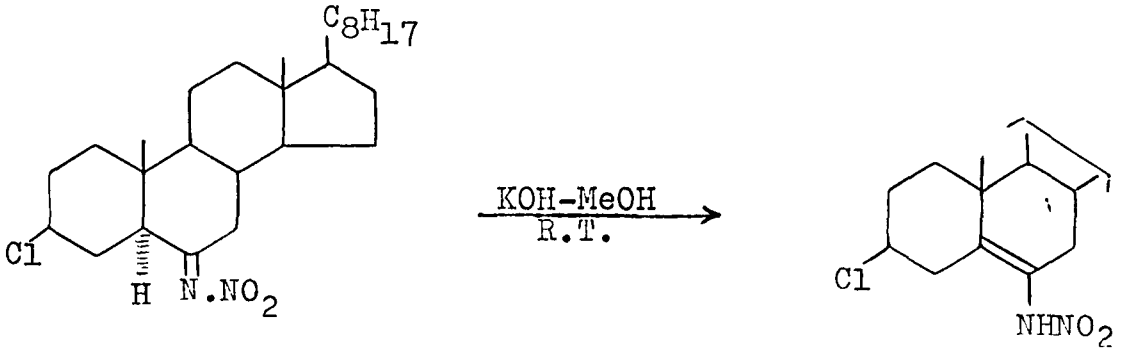
The compound m.p. 185° analysed for $C_{27}H_{46}O_2$. The IR spectrum of the compound m.p. 185° showed a broad absorption band at 3360-3400 cm^{-1} for O-H absorption. A strong band at 1710 cm^{-1} indicated the presence of a carbonyl group.

The NMR spectrum of the compound exhibited a multiplet at δ 3.7 ($W\frac{1}{2}$ = 6 Hz) which was assigned to the $C_7\beta$-H (equatorial). The methyl proton signals were observed at δ 0.93, 0.81, 0.73 and 0.63.

On the basis of the above spectral properties, the compound m.p. 185° was tentatively characterized as 6-oxo-7α-hydroxy-5α-cholestane (CCII).

Isomerization of 6-nitrimino-5α-cholestan-3β-yl chloride (CLXVIII)

The isomerization of the nitrimine (CLXVIII) with potassium hydroxide in methanol at room temperature afforded after usual work up and chromatography over silica gel, a compound having m.p. 165°.



(CLXVIII) (CCIII)

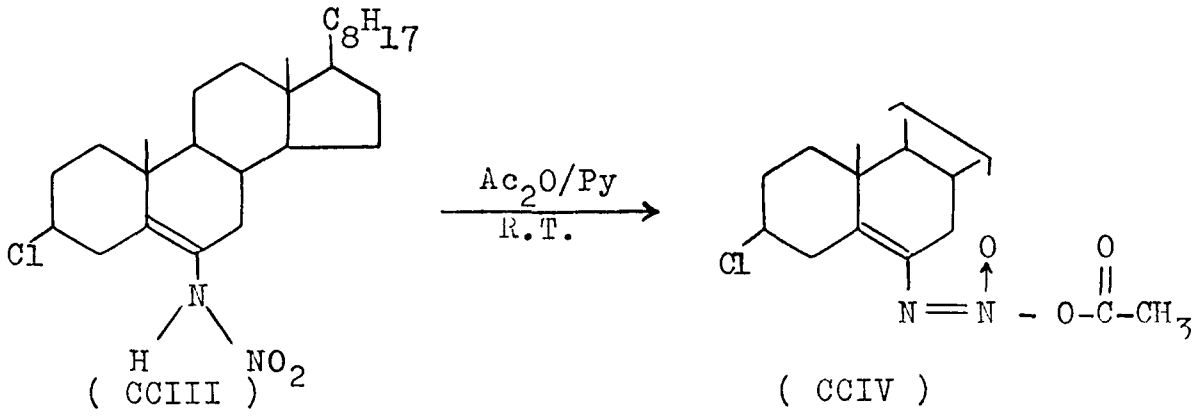
Characterization of the compound m.p. 165° as 6-nitroamino-cholest-5-en-3β-yl chloride (CCIII)

The compound (CCIII), m.p. 165° analysed for $C_{27}H_{45}N_2O_2Cl$. It gave positive Beilstein test, thereby showing that substitution or elimination of chlorine has not occurred.

The IR spectrum of the compound m.p. 165° exhibited bands which were characteristic of the nitroenamine function, i.e. 3480 m(N-H), 1620 w(C=C), 1570 s(ν_{as} NO_2) and 1310 s($\nu_s NO_2$) cm^{-1}. It also showed a medium band at 750 cm^{-1} for the C-Cl stretching vibrations.

The NMR spectrum of the compound (CCIII) showed a broad signal at δ 8.5 for the N<u>H</u>, a multiplet at δ 3.65 ($W\frac{1}{2}$ = 14 Hz) for the $C_3\alpha$-<u>H</u> and the methyl proton signals at δ 0.90, 0.81 and 0.71. The compound m.p. 165° was thus characterized as 6-nitroaminocholest-5-en-3β-yl chloride (CCIII) on the basis of the above mentioned spectral properties.

Acetylation of the nitroenamine (CCIII) with acetic anhydride and pyridine gave the O-acetyl derivative (CCIV) as a non-crystallizable oil.



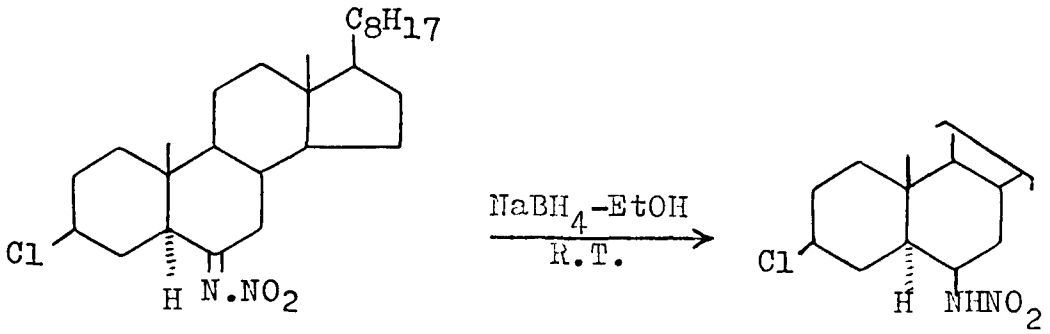
(CCIII) (CCIV)

The following spectral data for N-oxidoacetate (CCIV) were obtained.

$\nu_{max.}$ 1740 s(O-$\overset{O}{\overset{\|}{C}}$-$CH_3$), 1610 w(C=C), 1570 w(-N=N→O)[120], 1240 s, 1030 m(acetate) and 735 m(C-Cl) cm^{-1}; δ 3.8, ($C_3\alpha$ H, $W\frac{1}{2}$ = 17 Hz) 2.12 s(CH_3COO), 1.1, 0.91, 0.83 and 0.7 (methyl protons).

Reduction of 6-nitrimino-5α-cholestan-3β-yl chloride (CLXVIII)

Reduction of the nitrimine (CLXVIII) with sodium borohydride in absolute ethanol at room temperature afforded, after usual work up and evaporation of the solvent, a non-crystallizable oil.



(CLXVIII) (CCV)

Characterization of the oil as 6β-nitroamino-5α-cholestan-3β-yl chloride (CCV)

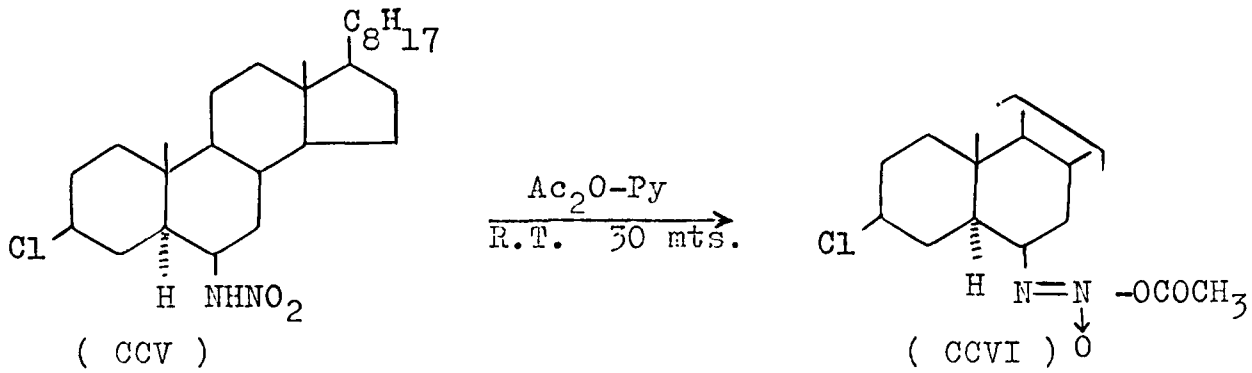
The oily compound obtained on reduction of the nitrimine (CLXVII) analysed for $C_{27}H_{47}N_2O_2Cl$. It gave positive Beilstein test.

The IR spectrum of the compound (CCV) exhibited bands which are characteristic of a nitramine function. It gave bands at 3485 m(NH) 1560 s(ν_{as} NO_2), 1310 s(ν_s NO_2) and 740 m(C-Cl)cm^{-1}. The NMR spectrum of the compound showed signals at δ 8.8 d(N<u>H</u>, J = 9 Hz), 4.2 m($C_6\alpha$-<u>H</u>, $W\frac{1}{2}$ = 6 Hz)[56], 3.7 m($C_3\alpha$-<u>H</u>, $W\frac{1}{2}$ = 14 Hz), 0.93, 0.8, 0.75 and 0.6 (methyl protons). The half-band width of the signal for C_6H was indicative of the fact that the nitramine group at C_6 was β-oriented (axial).

Reaction of the nitroamine (CCV) with acetic anhydride-pyridine

The reaction of (CCV) with acetic anhydride-pyridine at room temperature for 30 minutes, afforded after usual work up a non-crystallizable oil. It analysed for $C_{29}H_{49}N_2O_3Cl$ and gave positive Beilstein test. The IR spectrum of the oil exhibited prominent bands at 1735 s, 1570 w, 1240 s, 1030 m and 750 m cm^{-1}. The spectrum was however, conspicuous by the absence of strong bands for the nitro group (1570-1550 and 1340-1320 cm^{-1}). The NMR spectrum exhibited signals at δ 4.4 m ($C_6\alpha$-<u>H</u>; $W\frac{1}{2}$ =7 Hz), 3.7 m($C_3\alpha$-<u>H</u>, $W\frac{1}{2}$ = 16 Hz), 0.93, 0.81, 0.7, 0.63

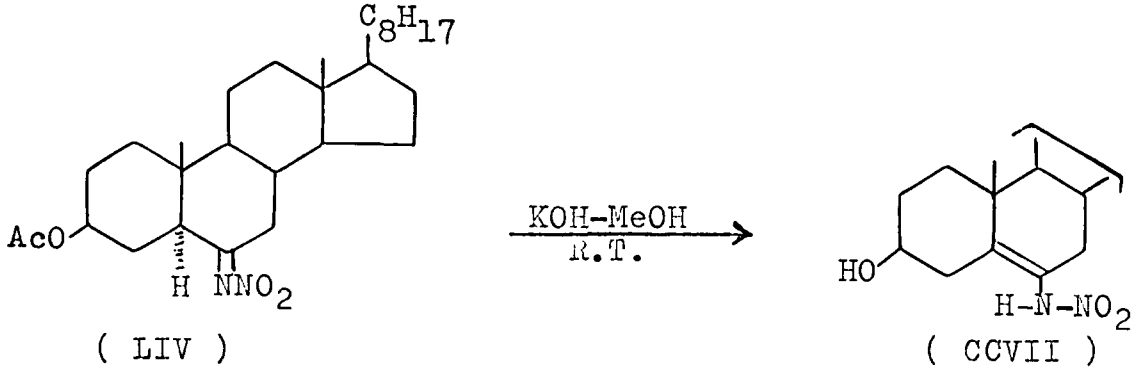
(other methyl protons). These spectral values suggest an N-oxidoacetate structure (CCVI) for the compound.



(CCV) (CCVI)

Isomerization of 6-nitrimino-5α-cholestan-3β-yl acetate (LIV)

The treatment of the nitrimine (LIV) with potassium hydroxide in methanol resulted in the formation of a single product having m.p. 158°.



(LIV) (CCVII)

Characterization of the compound m.p. 158° as 6-nitroamino-cholest-5-en-3β-ol (CCVII)

The compound m.p. 158° analysed for $C_{27}H_{46}N_2O_3$. It is clear from the anlysis that the acetate function has expectedly been hydrolyzed during the course of isomerization.

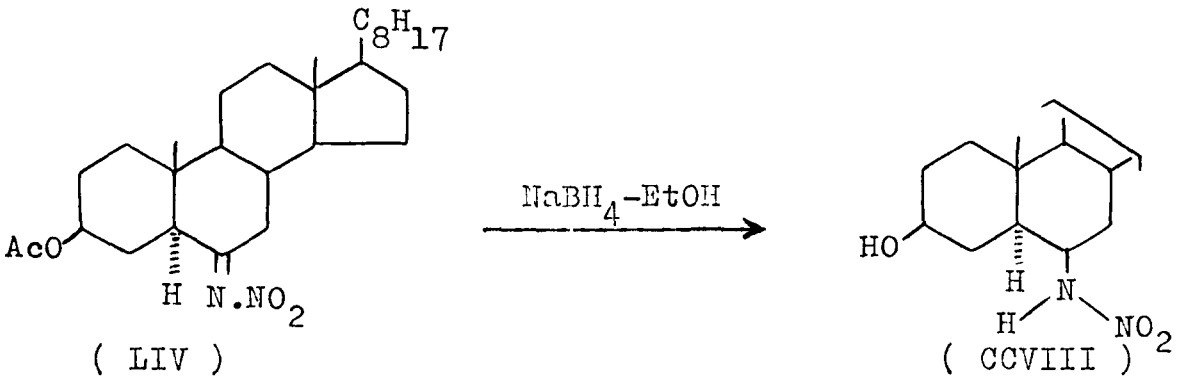
The IR spectrum of the compound did not show bands for the acetate carbonyl group. It however, showed a medium band at 3460-3500 which was due to the O-H and N-H absorptions. A medium band at 1600 cm^{-1} and strong bands at 1550 and 1320 cm^{-1} were due to the nitroenamine function.

The NMR spectrum of the compound (CCVII) showed a one proton signal at δ 8.6 which was assigned to the amine proton. A multiplet at δ 3.7 ($W\frac{1}{2}$ = 14 Hz) was due to the $C_3\alpha$-H while the methyl protons were observed at δ 0.93, 0.83, 0.7 and 0.63.

On the basis of these spectral values, the compound m.p. 158° was characterized as 6-nitroaminocholest-5-en-3β-ol (CCVII).

Reduction of 6-nitrimino-5α-cholestan-3β-yl acetate (LIV)

6-Nitrimino-5α-cholestan-3β-yl acetate (LIV) on treatment with sodium borohydride in ethanol, underwent reduction to furnish a compound having m.p. 192°.



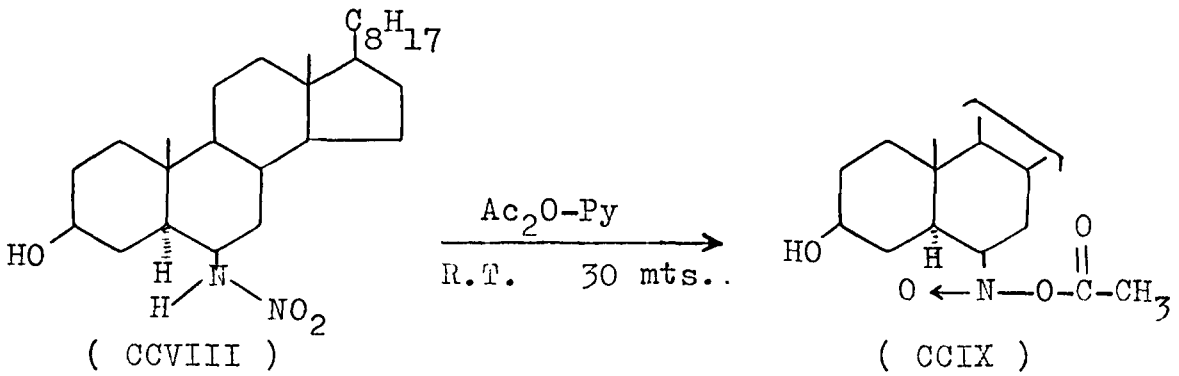
(LIV) (CCVIII)

Characterization of the compound m.p. 192° as 6-nitroamino-5α-cholestan-3β-ol (CCVIII)

The compound m.p. 192° analysed for $C_{27}H_{48}N_2O_3$. It is evident from the analysis that the acetate function has been hydrolyzed during the course of reduction.

The IR spectrum of the compound exhibited bands at 3400-3520 m(NH and OH), 1550 s(ν_{as} NO_2), 1320 s(ν_s NO_2) and 1030 m(C-O) cm^{-1}. These bands are characteristic of the nitroamine function. The NMR spectrum of the compound showed a doublet at δ 8.9 (J = 7 Hz) which was due to the amine proton. A multiplet at δ 4.15 ($W\frac{1}{2}$ = 6 Hz) was ascribed to the $C_6\alpha$-H (equatorial)[56] while another multiplet at δ 3.75 ($W\frac{1}{2}$ = 18 Hz) was assigned to the $C_3\alpha$-H. The methyl protons appeared at δ 0.93, 0.81, 0.7 and 0.63.

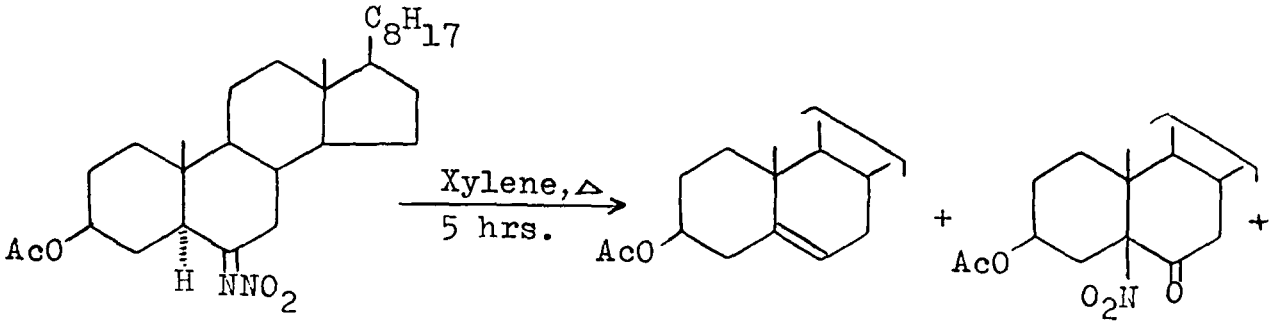
The nitroamine (CCVIII) on treatment with acetic anhydride-pyridine at room temperature for 30 minutes, afforded after usual work up, an oil which failed to crystallize. The oil analysed for $C_{29}H_{50}N_2O_4$. The IR spectrum of the compound showed bands at 3420 m(OH), 1735 s($CH_3-\overset{O}{\overset{\|}{C}}-O$), 1565 w($-N=\overset{+}{N}-\bar{O}$)[120], 1240 s and 1030 m(acetate) cm^{-1}. The spectrum was devoid of the strong bands for the nitro group. The NMR spectrum showed signals at δ 4.3 m($C_6\alpha$-$\underline{H}$, $W\frac{1}{2}$ = 7 Hz), 3.7 m($C_3\alpha$-$\underline{H}$, $W\frac{1}{2}$ = 16 Hz), 2.1 s($C\underline{H}_3COO$), 0.93, 0.8, 0.71 and 0.68 (other methyl protons). The acetylation of the OH group at C_3 would have provided a product with a very different spectral properties. Also prolonged acetylation was avoided as this would have resulted in denitro-amination[56]. On the basis of the above mentioned spectral properties the compound was assigned the N-oxidoacetate structure (CCIX).



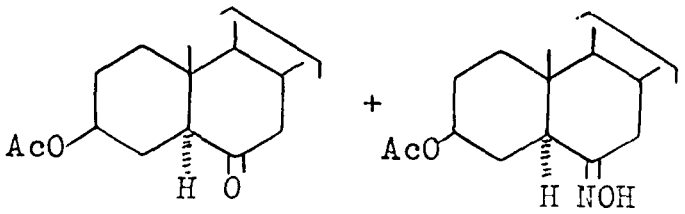
(CCVIII) (CCIX)

Thermolysis of 6-nitrimino-5α-cholestan-3β-yl acetate (LIV)

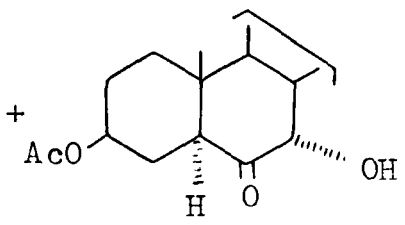
The nitrimine (LIV) on thermolysis in refluxing xylene for five hours, afforded after the removal of the solvent in vacuo, a dark brown oil which on column chromatography over silica gel afforded five compounds, m.pts. 115°, 75°, 127°, 200° and 235°.



(LIV) (CCX) (CCXI)



(CLXXI) (CLXX)



(CCXIII)

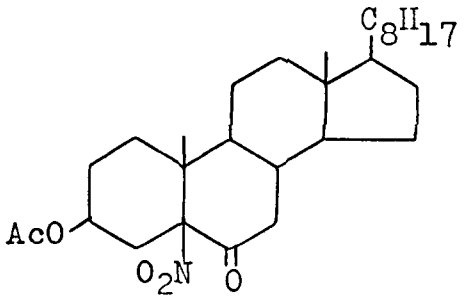
Characterization of the compound m.p. 115° as cholest-5-en-3β-yl acetate (CCX)

The compound m.p. 115° was characterized as cholest-5-en-3β-yl acetate (CCX) on the basis of its spectral data [$\nu_{max.}$ 1725 s(CH_3COO), 1620 m(C=C), 1240 m(acetate), 1030 m(C-O) cm^{-1}; δ 5.35 m(C_6-vinylic H), 4.74 m($C_3\alpha$ H, $W_{\frac{1}{2}}$ = 16 Hz), 1.95 s(CH_3COO), 1.1, 0.91, 0.83 and 0.68 (methyl protons)] and by comparison with an authentic sample[122] of (CCX).

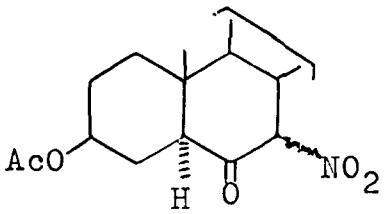
Characterization of the compound m.p. 75° as 6-oxo-5β-nitro-cholestan-3β-yl acetate (CCXI)

The compound m.p. 75° analysed for $C_{29}H_{47}NO_5$ (M^+ 489).

The IR spectrum of the compound (CCXI) exhibited prominent bands at 1730, 1700, 1580, 1370 and 1240 cm^{-1}. The two strong bands at 1730 and 1700 cm^{-1} were ascribed to the acetate carbonyl and C_6 carbonyl groups, respectively. The bands at 1580 and 1370 cm^{-1} were characteristic for the unsymmetrical and symmetrical stretching vibrations of the nitro group. It is thus evident from these values that the compound has an acetate function at C_3, a carbonyl group, most probably, at C_6 and a nitro group in the near vicinity, say at either C_5 or C_7 as in structures (CCXI) and (CCXII), respectively.



(CCXI)



(CCXII)

The distinction between these two structures and the assignment of structure (CCXI) to the compound m.p. 75° was based on the NMR spectrum of the compound. It showed a multiplet at δ 5.05 integrating for one proton which was assigned to the $C_3\alpha$-H. The half-band width of the C_3H signal (6 Hz) was indicative of the fact that the ring junction A/B has changed to cis. Also there was no signal in the NMR spectrum compatible with C_7-H as required by the structure (CCXII). These spectral data support the structure (CCXI) for the compound m.p. 75° which has been tentatively characterized as 6-oxo-5β-nitrocholestan-3β-yl acetate (CCXI).

The structure (CCXI) for the compound m.p. 75° was further supported by its mass spectrum which gave a very small molecular ion peak at m/z 489. The molecular ion peak was followed by some significant fragment ions at m/z 443 (M^+-NO_2), 442 (M^+-HNO_2) and 383 (M^+-NO_2+AcOH), which support the proposed structure(CCXI) for the nitro compound.

Characterization of the compound m.p. 127° as 6-oxo-5α-cholestan-3β-yl acetate (CLXXI)

The compound m.p. 127° was identified as 6-oxo-5α-cholestan-3β-yl acetate (CLXXI) on the basis of its spectral data and its comparison with an authentic sample of the ketone[104].

Characterization of the compound m.p. 200° as 6-oximino-5α-cholestan-3β-yl acetate (CLXX)

The compound m.p. 200° was characterized as 6-oximino-5α-cholestan-3β-yl acetate (CLXX) on the basis of its spectral properties and by comparison with an authnetic sample of the oxime[103].

Characterization of the compound m.p. 235° as 6-oxo-7α-hydroxy-5α-cholestan-3 β-yl acetate (CCXIII)

The compound m.p. 235° analysed for $C_{29}H_{48}O_4$(M^+460).

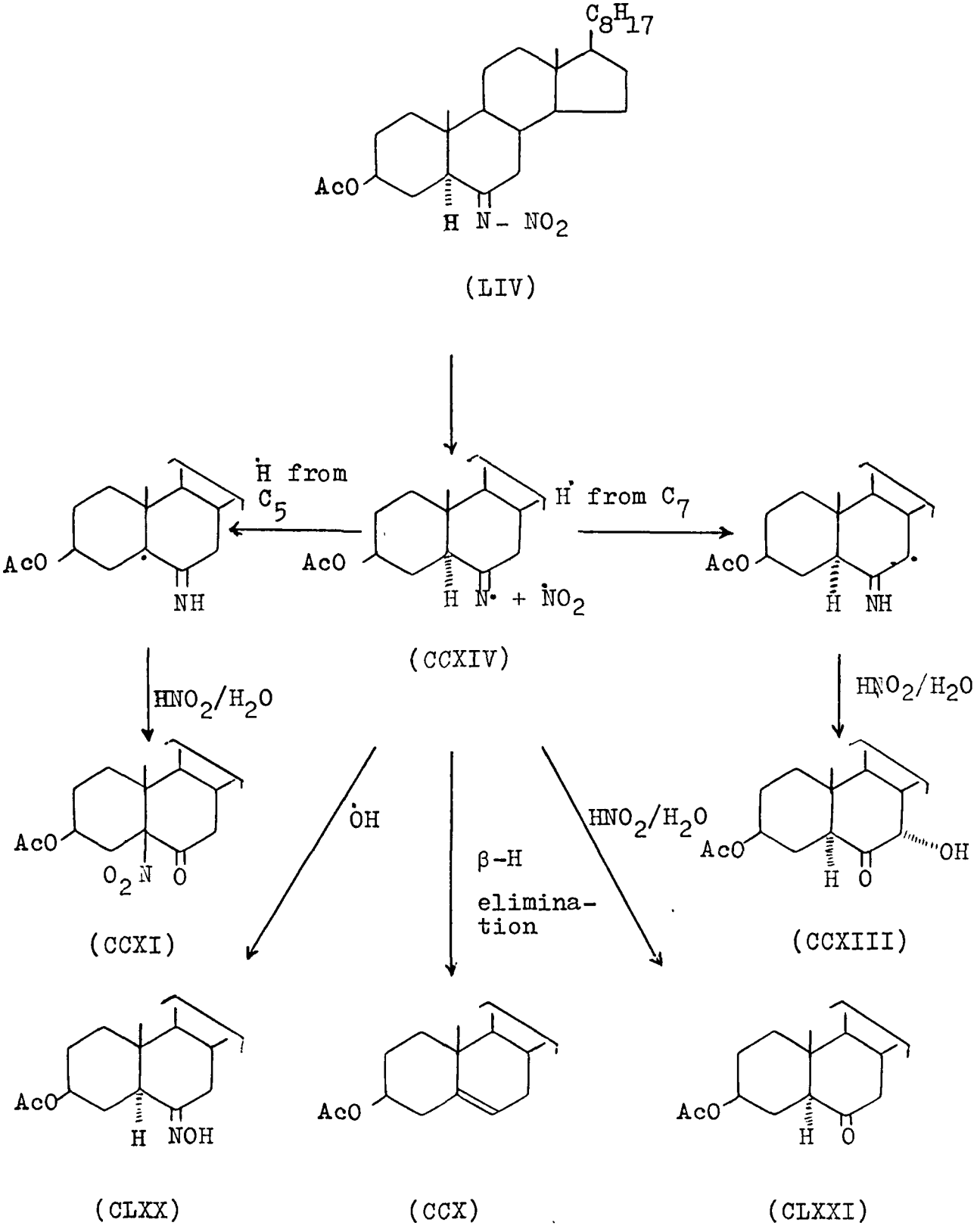
The IR spectrum of the compound exhibited absorption bands at 3430, 1725, 1701, 1240 and 1040 cm^{-1}. The broad band at 3430 was probably due to the OH stretching vibrations. The two strong bands at 1725 and 1701 cm^{-1} were assigned to the C_3-acetate carbonyl and C_6-carbonyl groups, respectively. The medium bands at 1240 and 1040 cm^{-1} were due to acetate and C-O. The compound m.p. 235° thus, has a hydroxy group either at C_5 or at C_7 besides the C_3-acetate and C_6-carbonyl functions.

The NMR spectrum of the compound exhibited a broad multiplet at δ 4.8 ($W\frac{1}{2}$ = 14 Hz) which was ascribed to the $C_3\alpha$-H. A multiplet at δ 3.75 ($W\frac{1}{2}$ = 5 Hz) was assigned to the $C_7\beta$-H (equatorial) and was indicative of the fact that the hydroxyl group in the compound was attached to C_7 rather than C_5. The half-band width of the signal for C_7H indicated that the hydroxyl group was α-oriented (axial). The compound m.p. 235° was thus tentatively characterized as 6-oxo-7α-hydroxy-5α-cholestan-3β-yl acetate (CCXIII).

The structure (CCXIII) found further support from the mass spectrum of the compound which showed a molecular ion peak at m/z 460, followed by some significant fragment ions at m/z 442 (M^+-H_2O), 400 (M^+-AcOH), 382 (400-H_2O) and 372 (400-CO), which have a bearing on the structure of the hydroxy compound (CCXIII).

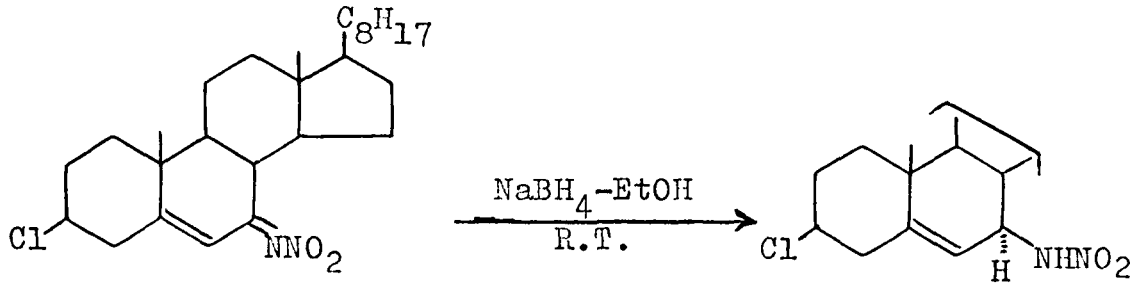
The mechanistic pathways involved in the formation of different products of thermolysis of the nitrimine (LIV) have been shown in scheme 13. The initial phase of the reaction most probably occurs through the homolytic cleavage of N-NO_2 bond[67] to give the radical (CCXIV). This radical then rearranges differently to give the appropriate products. The abstraction of a hydrogen by NO_2 radical would also produce HNO_2 which may break up to give NO, NO_2 and H_2O. The olefin (CCX) is formed from the nitrimine (LIV) by denitroimination by hydrogen β-elimination.

Scheme 13


C_8H_{17}
AcO
H N- NO_2
(LIV)
H from C_5
H from C_7
AcO
NH
H N· + $\dot{N}O_2$
H NH
(CCXIV)
HNO_2/H_2O
HNO_2/H_2O
AcO
O_2N O
(CCXI)
ȮH
β-H elimination
HNO_2/H_2O
AcO
OH
H O
(CCXIII)
AcO
H NOH
(CLXX)
AcO
(CCX)
AcO
H O
(CLXXI)

Reduction of 7-nitriminocholest-5-en-3 β-yl chloride (CLXXXVII)

Reduction of the nitrimine (CLXXXVII) with sodium borohydride in absolute ethanol afforded a single compound having m.p. 137°.



(CLXXXVII) (CCXV)

Characterization of the compound m.p. 137° as 7β-nitroaminocholest-5-en-3β-yl chloride (CCXV)

The compound m.p. 137° analysed for $C_{27}H_{45}N_2O_2Cl$. It gave positive Beilstein test.

The IR spectrum of the compound m.p. 137° showed bands which were characteristic of the nitroamine function. The bands were observed at 3420 m(N-H), 1620 m(C=C), 1550 s(ν_{as} NO_2), 1330 s(ν_s NO_2) and 750 m(C-Cl). The NMR spectrum of the compound exhibited a vinylic proton signal at δ 5.26. A multiplet at δ 4.3 ($W\frac{1}{2}$ = 8 Hz) was ascribed to the C_7α-H (axial)[56] while another multiplet at δ 3.7 ($W\frac{1}{2}$ = 16 Hz) was assigned to the

$C_3\alpha$-H. Methyl protons appeared at δ 1.1, 0.91, 0.83 and 0.7.

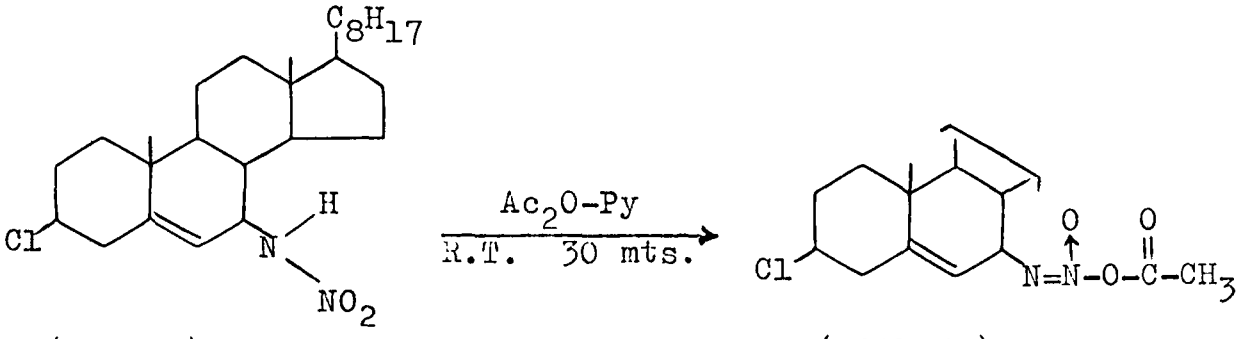
On the basis of these spectral properties the compound m.p. 137° was characterized as 7β-nitroaminocholest-5-en-3β-yl chloride (CCXV).

Reaction of the nitroamine (CCXV) with acetic anhydride-pyridine

The nitroamine (CCXV) on reaction with acetic anhydride-pyridine furnished, after usual work up, a non-crystallizable oil. It analysed for $C_{29}H_{47}N_2O_3Cl$ and gave positive Beilstein test.

The IR spectrum of the compound exhibited significant bands at 1730 s(CH_3-$\underset{\underset{O}{\|}}{C}$-O), 1610 w(C=C), 1565 w(-N=$\overset{+}{N}$-$\bar{O}$)[120], 1240 s, 1030 m(acetate) and 750 m (C-Cl) cm^{-1}. The two strong bands at 1570-1550 and 1340-1320 cm^{-1} for the nitro group were conspicous by their absence.

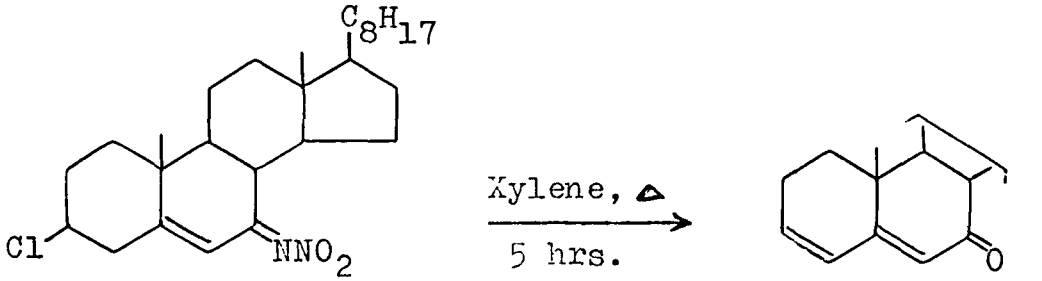
The NMR spectrum exhibited a vinylic proton doublet at δ 5.6 (J = 6 Hz) which was assigned to C_6-H. A multiplet at δ 4.8 ($W\frac{1}{2}$ = 8 Hz) was due to the $C_7\alpha$-H (axial). The $C_3\alpha$-H appeared at δ 3.75 as a multiplet ($W\frac{1}{2}$ = 17 Hz) while the acetate methyl was observed at δ 1.97. The signals at δ 1.1, 0.9, 0.8 and 0.71 were assigned to other methyl protons. These spectral values are in full agreement with the N-oxidoacetate structure (CCXVI) assigned to the oil.



(CCXV) (CCXVI)

Thermolysis of 7-nitriminocholest-5-en-3β-yl chloride (CLXXXVII)

Thermolysis of the nitrimine (CLXXXVII) in xylene afforded after the evaporation of the solvent in vacuo, a brown oil which on column chromatography over silica gel gave a compound m.p.112°.



(CLXXXVII) (CLXXXIX)

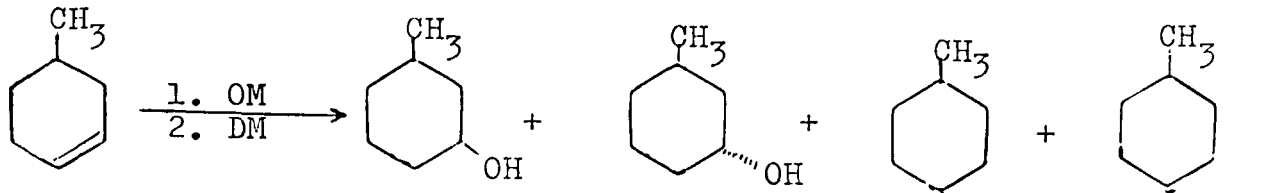
Characterization of the compound m.p. 112° as 7-oxocholesta-3,5-diene (CLXXXIX)

The compound m.p. 112° was characterized as 7-oxocholesta-3,5-diene (CLXXXIX) on the basis of its spectral properties and by comparison with an authentic sample of the dienone[114].

PART - THREE

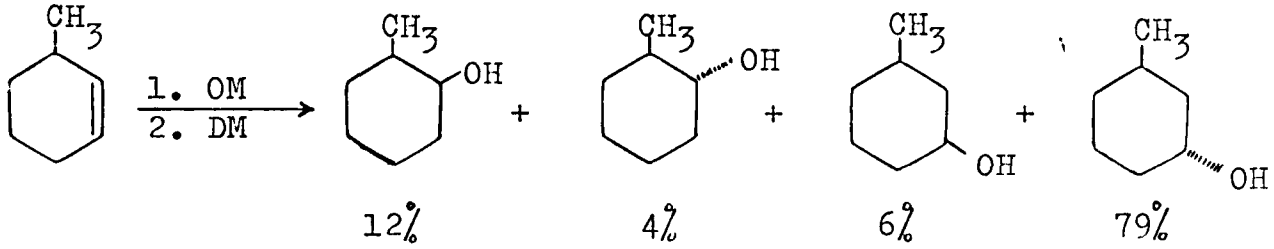
A. OXYMERCURATION-DEMERCURATION OF STEROIDAL OLEFINS

The oxymercuration-demercuration procedure provides a convenient synthetic method for affecting the Markownikoff hydration of a carbon-carbon double bond[123-125]. In case of unhindred acylic olefins the oxymercuration reaction usually proceeds with no rearrangements and amazingly high regioselectivity. In case of conformationally rigid cyclic systems[126], however, the results are quite different. The effects of substitution on the course of oxymercuration reactions has also been visualized in some cases[127]. 4-Methylcyclohexene (CCXVII), for example, undergoes oxymercuration-demercuration in a remarkebly stereoslective but non-regioselective manner to give a mixture of cis- and trans- isomers.



(CCXVII) 1% (CCXVIII) 47% (CCXIX) 51% (CCXX) 1% (CCXXI)

On the other hand 3-methylcyclohexene (CCXXII) undergoes hydration in a regio- and stereoselective manner, favouring the trans-3-methylcyclohexanol (CCXIX) because of torsional effects.



12% 4% 6% 79%

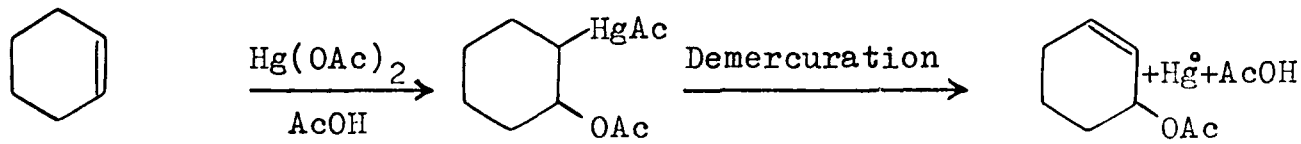
(CCXXII) (CCXXIII) (CCXXIV) (CCXVIII) (CCXIX)

The presence or absence of regio- and stereoselectivity is thus, intricately dependent upon the nature of the olefin and size and position of the substituents.

The oxymercuration-demercuration of a number of strained olefins[128,129] has been carried out and it has been observed that the addition is cis if the olefin is strained and bicyclic[128-130]. The oxymercuration occurs in cis manner with norbornenes[130-133], both cis and trans with bicyclo [2.2.2] octene[134] and trans with cyclohexene or rather simple cyclic olefins[130-132].

The oxymercuration-demercuration sequence has also been used for affecting allylic oxidation of olefins. Such an oxidation is a part of the general oxidation of alkenes by the salts of multivalent metals. These reactions first give stable mercury adducts[135] which on demercuration lead to an allylic compound depending upon the structure of the olefin, the nature

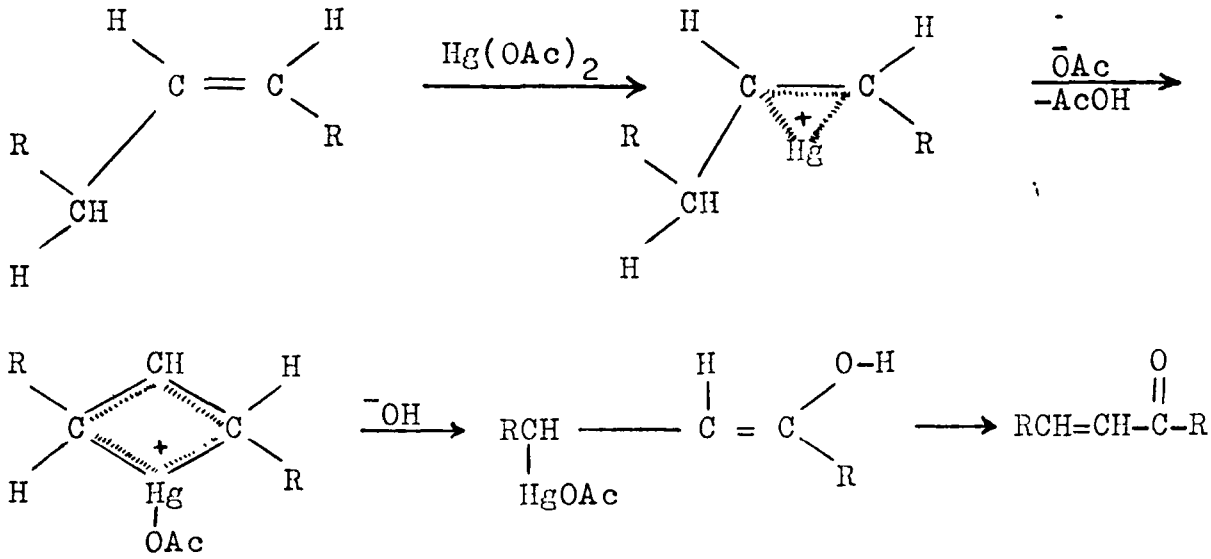
of the medium and the time of the reaction[136-138]. Cyclohexene (CCXXV) for example, undergoes oxymercuration-demercuration in acetic acid to give metallic mercury and allylic acetate (CCXXVI)[139].



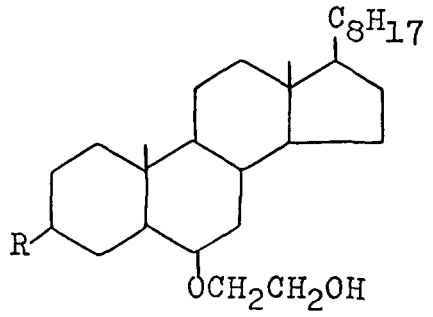
(CCXXV) (CCXXVI)

In some cases the formation of α,β-unsaturated ketones has also been reported by oxymercuration-demercuration reactions. The formation of such compounds during these reactions have been explained by the involvement of allylic π-complex[140] (Scheme 14).

Scheme 14



A survey of the literature revealed that the oxymercuration-demercuration reaction has not been studied in the field of steroids to a significant extent. A number of steroidal hydroxyethers such as (CCXXVII-CCXXXI) were prepared in our laboratory[141-144] by mixed hydride reduction of cyclic ketals as shown in the scheme 15.

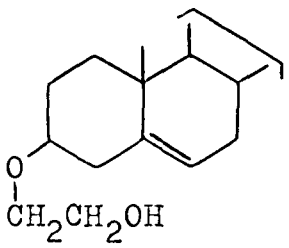


R

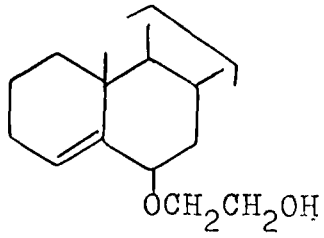
(CCXXVII) H

(CCXXVIII) OH

(CCXXIX) Cl

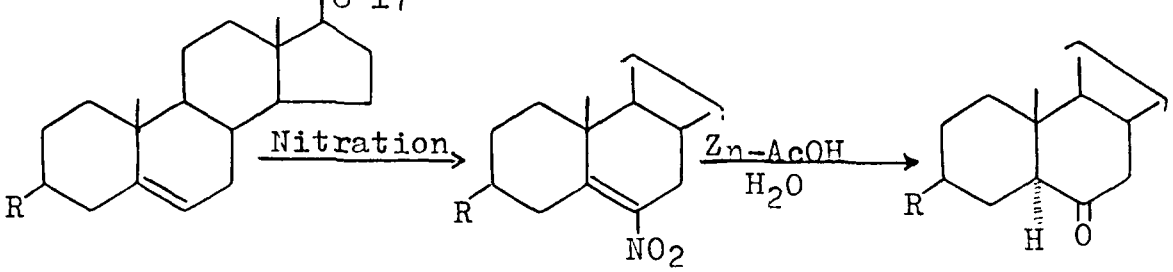


(CCXXX)



(CCXXXI)

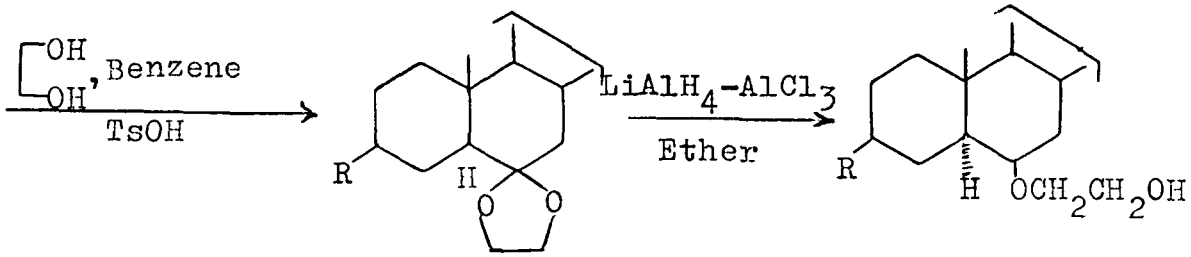
Scheme 15



(CCI) R = H

(CCX) R = OAc

(CCXXXII) R = Cl



R

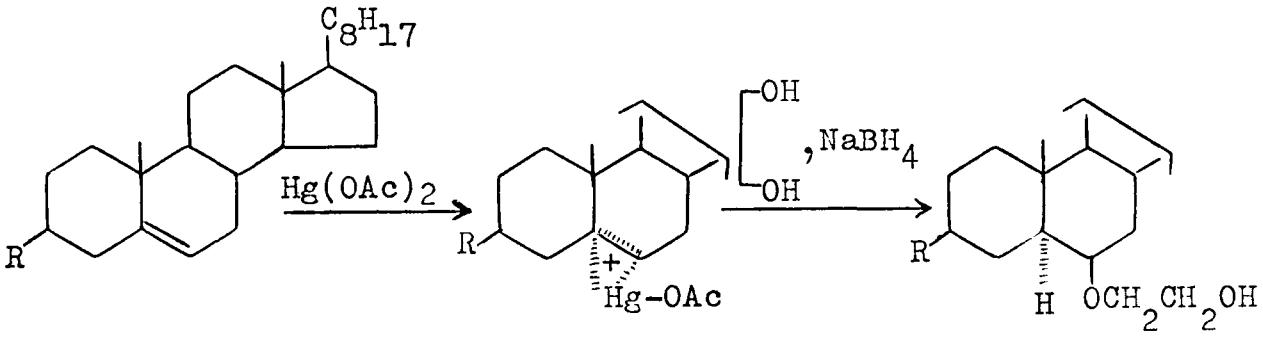
(CCXXVII) H

(CCXXVIII) OH

(CCXXIX) Cl

It was hopefully visualized that such hydroxy ethers can also be obtained by the oxymercuration-demercuration method starting from steroidal olefins (CCI), (CCX) and (CCXXXII) according to the scheme 16, which would involve lesser number of steps.

Scheme 16



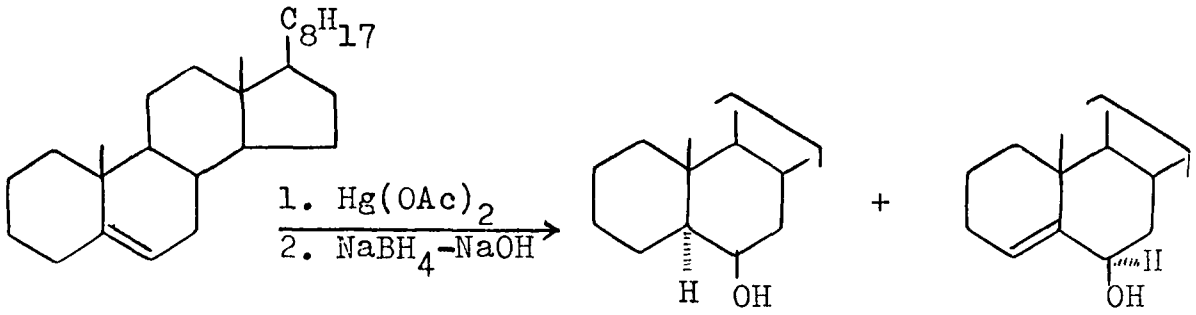
	R
(CCI)	H
(CCX)	OAc
(CCXXXII)	Cl

	R
(CCXXVII)	H
(CCXXVIII)	OH
(CCXXIX)	Cl

Keeping these points in view we have carried out the oxymercuration-demercuration reaction of some of the easily accessible steroidal olefins, such as cholest-5-ene (CCI) and cholest-5-en-3β-yl chloride (CCXXXII). The oxymercuration has, in all cases been carried out by mercuric acetate in acetic acid under refluxing conditions while the demercuration has been effected with sodium borohydride in different reaction media.

Oxymercuration-demercuration of cholest-5-ene (CCI) using $Hg(OAc)_2$-$NaBH_4$-NaOH

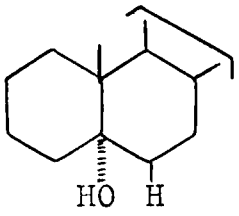
Oxymercuration of cholest-5-ene (CCI) with mercuric acetate in acetic acid gave the organomercury acetate adduct which on demercuration with sodium borohydride in sodium hydroxide solution afforded, after usual work up and chromatography over silica gel, two compounds, m.pts. 80° and 140°.



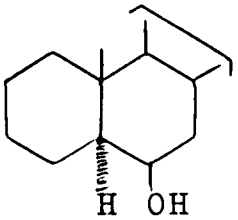
(CCI) (CCXXXIV) (CCXL)

Characterization of the compound, m.p. 80° as 5α-cholestan 6β-ol (CCXXXIV)

The compound, m.p. 80°, analysed for $C_{27}H_{48}O$. It is evident from this analysis that the olefin (CCI) has undergone hydration during the course of oxymercuration-demercuration reaction. Two possible structures compatible with this analysis may be either the Markownikoff hydration product (CCXXXIII) or the anti-Markownikoff product (CCXXXIV).



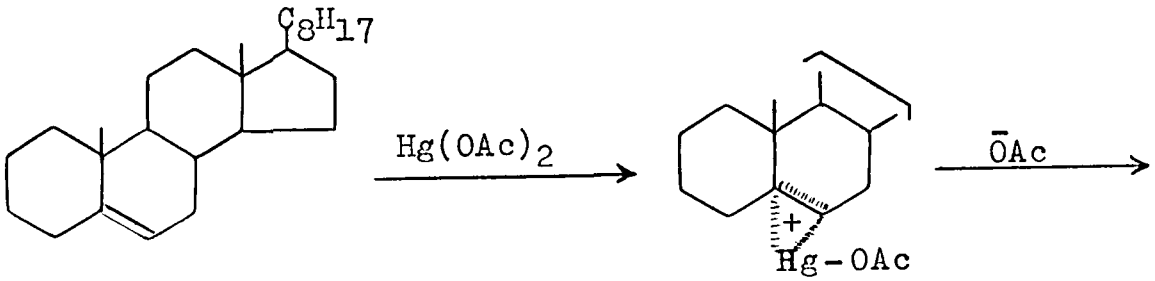
(CCXXXIII)



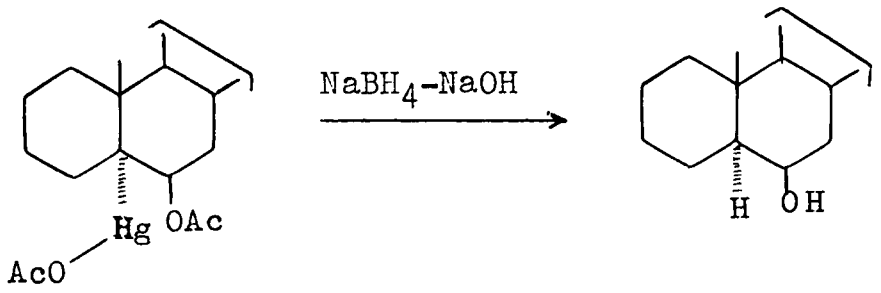
(CCXXXIV)

The IR spectrum of the compound m.p. 80° showed a broad absorption band due to O-H stretching frequency at 3410 cm^{-1}. The broad band was indicative of the fact that the hydroxy group may be hydrogen bonded secondary as in (CCXXXIV) rather than tertiary as in (CCXXXIII), which would have a sharp absorption band.

The conclusive distinction between the isomeric alcohols (CCXXXIII) and (CCXXXIV) was however, made on the basis of the NMR spectrum of the compound which exhibited a multiplet ($W\frac{1}{2}$ = 6 Hz) at δ 3.7 which was assigned to the $C_6\alpha$-H (equatorial). The isomer (CCXXXIII) having the OH at C_5 would not give such a signal in its spectrum. The half band width of the $C_6\underline{H}$ indicated that the OH group at C_6 was β-oriented i.e., axial. The β-orientation of the hydroxy group at C_6 is also justified on mechanistic grounds. The oxymercuration results in the formation of cyclic organomercury acetate adduct (CCXXXV). The cyclic intermediate then opens trans diaxially to give acetoxymercury acetate (CCXXXVI). The demercuration of (CCXXXVI) with sodium hydroxide and sodium borohydride gives the alcohol (CCXXXIV).

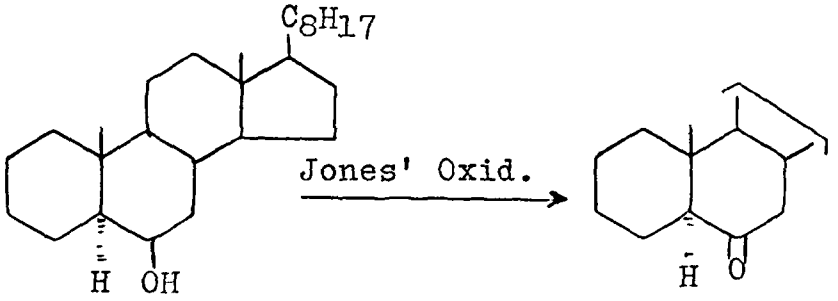


(CCI) (CCXXXV)



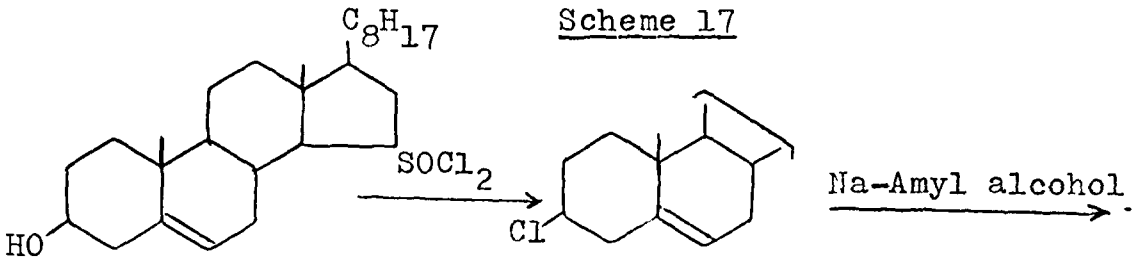
(CCXXXVI) (CCXXXIV)

A mixed m.p. determination of the compound with an authentic sample[145] of (CCXXXIV) gave no depression. The chemical support for the structure (CCXXXIV) for the compound m.p. 80° was obtained by its Jones' oxidation which furnished 6-oxo-5α-cholestane (CLXIV), identified on the basis of its spectral properties and comparison with an authentic sample of the ketone (CLXIV) prepared by the literature procedure[100] as shown in scheme 17.

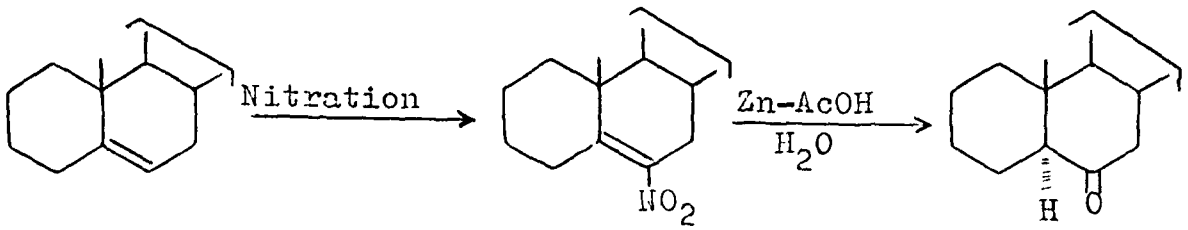


(CCXXXIV) (CLXIV)

Scheme 17



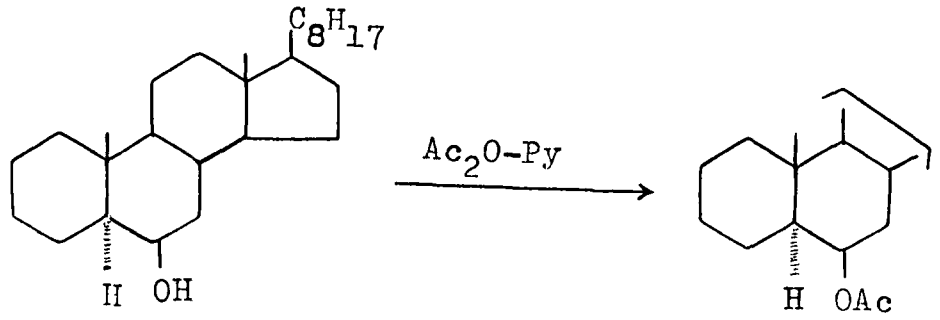
(CCXXXVII) (CCXXXII)



(CCI) (CCL) (CLXIC)

Further chemical support for the structure of the compound m.p. 80° as (CCXXXIV) rather than (CCXXXIII) was obtained by its acetylation with acetic anhydride and pyridine. The acetylation of the compound occurred and resulted in the formation of 5α-cholestan-6β-yl acetate (CCXXXVIII). The acetate (CCXXXVIII)

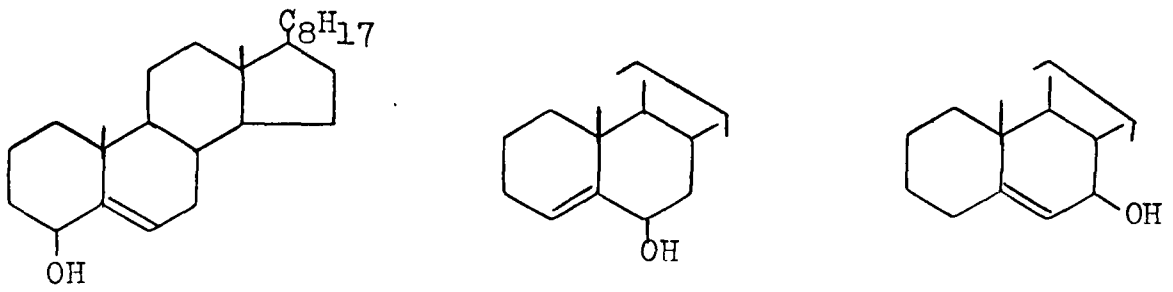
was identified on the basis of its spectral properties [$\nu_{max.}$ 1735 s(CH_3-C(=O)-O), 1240 m(acetate), 1030 m(C-O) cm^{-1}; δ 4.6 m($C_6\alpha$-H, $W\frac{1}{2}$ = 6 Hz), 2.1 s(CH_3COO), 0.97, 0.91, 0.81 and 0.67 (methyl protons)].



(CCXXXIV) (CCXXXVIII)

Characterization of the compound m.p. 140° as cholest-4-en-6β-ol (CCXL)

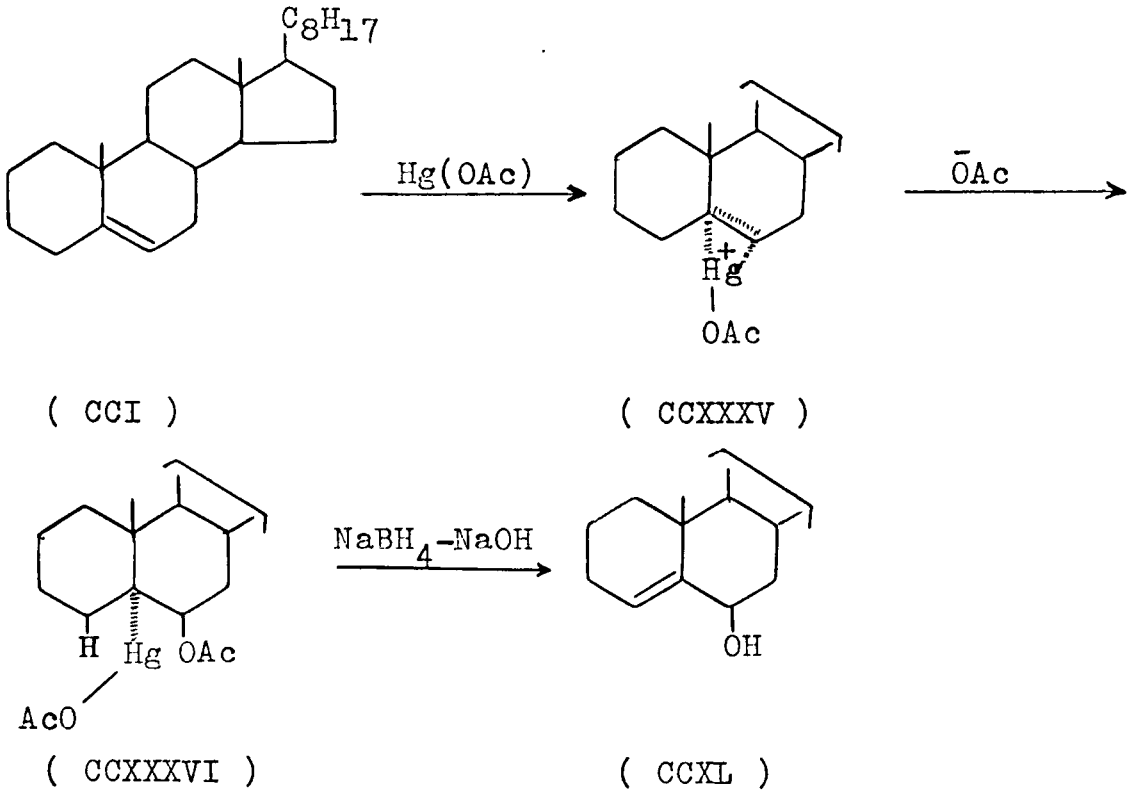
The compound m.p. 140° analysed for $C_{27}H_{46}O$. It is evident from the analysis that an oxygen atom has been added to the starting olefin (CCI), most probably as an OH group to form an allylic alcohol. Three possible structures compatible with the analysis are (CCXXXIX), (CCXL) and (CCXLI).



(CCXXXIX) (CCXL) (CCXLI)

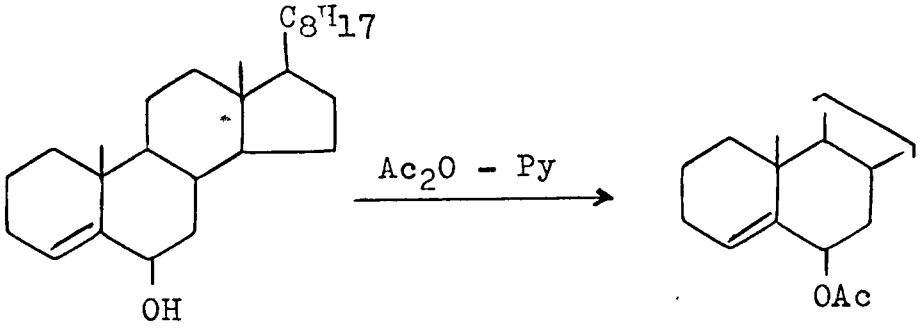
The IR spectrum of the compound m.p. 140° exhibited a strong OH absorption band at 3500 cm^{-1}. A weak band at 3030 cm^{-1} and a medium band at 1650 cm^{-1} indicated the presence of carbon-carbon double bond in the compound and it was therefore thought that the compound m.p. 140° must have been formed by allylic oxidation of the olefin (CCI).

Of the three possible allylic alcohols, the formation of (CCXXXIX) and (CCXLI) can not be accounted for on mechanistic grounds, as the first step in oxymercuration reaction is the attack of mercury salt on the carbon-carbon double bond to give organomercury acetate adduct. Demercuration of the adduct is accompanied with the rearrangement to give allylic acetate or alcohol depending upon the reaction media.



The structure of the compound m.p. 140° was supported by its NMR spectrum which exhibited a vinylic proton signal at δ 5.61 as multiplet ($W\frac{1}{2}$ = 12 Hz) which was assigned to C_4-H. A multiplet for C_6H was observed at δ 3.9 ($W\frac{1}{2}$ = 6 Hz) which suggested that the $C_6\underline{H}$ is equatorial (α-oriented).

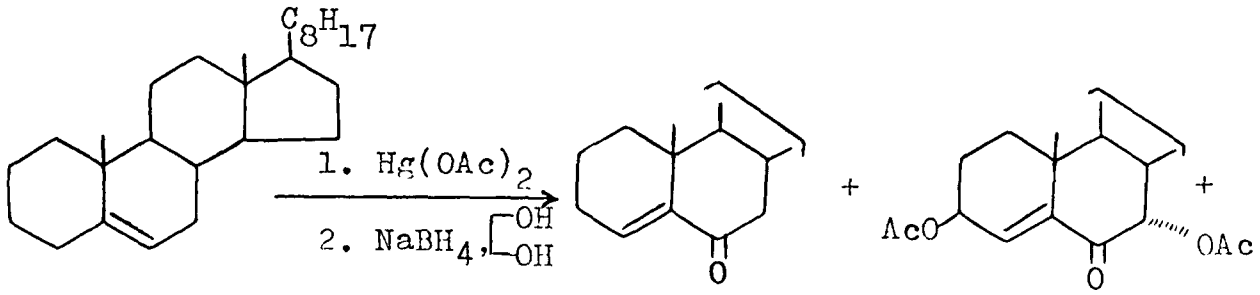
The chemical support for structure (CCXL) was obtained from the acetylation of the compound with acetic anhydride and pyridine, which gave cholest-4-en-6β-yl acetate (CCXLII). The acetate (CCXLII) was identified on the basis of its spectral data [$\nu_{max.}$ 3030 w(C=C-H), 1730 s(CH_3COO), 1240 m(acetate), 1030 m(C-O) cm^{-1}; δ 5.7 m(C_4-vinylic $\underline{H}$), 4.8 m($C_6\underline{H}$, $W\frac{1}{2}$ = 6 Hz), 2.01 s($C\underline{H}_3COO$), 0.98, 0.9, 0.8 and 0.7 (methyl protons)].



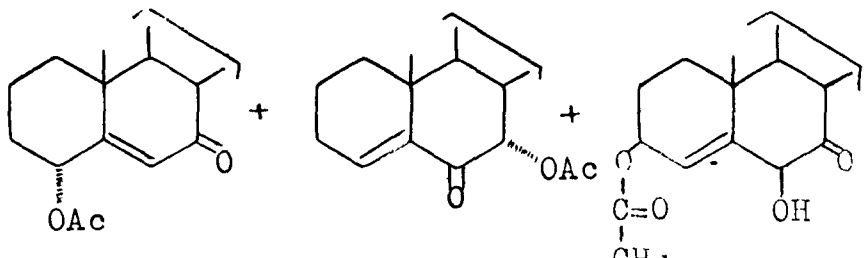
(CCXL) (CCXLII)

Oxymercuration-demercuration of cholest-5-ene (CCI) using $Hg(OAc)_2$-$NaBH_4$-Ethylene Glycol

Oxymercuration of cholest-5-ene (CCI) with mercuric acetate in acetic acid gave the organomercurial adduct which on demercuration with sodium borohydride in ethylene glycol medium furnished after usual work up and chromatography over silica gel, five different compounds. One of these was obtained as a solid having m.p. 105°, while the other four were obtained as non-crystallizable oils which for convenience, have been labelled as K-1, K-2, K-3 and K-4.



(CCI) (CCXLIII) (CCXLIV)



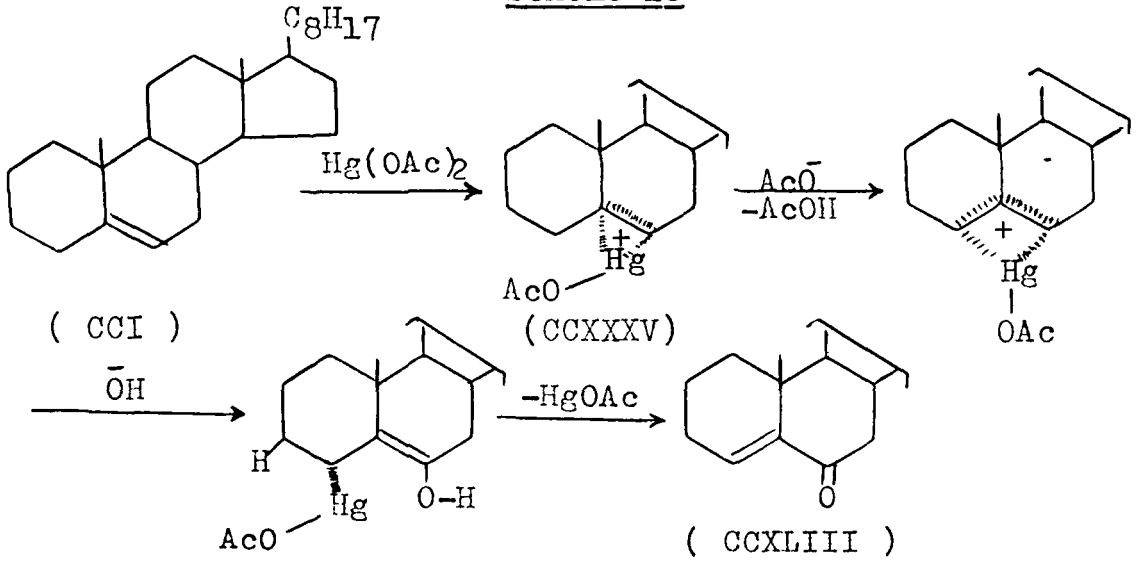
(CCXLV) (CCXLVI) (CCXLVII)

Characterization of the compound m.p. 105° as 6-oxocholest-4-ene (CCXLIII)

The compound m.p. 105° analysed for $C_{27}H_{44}O$. The IR spectrum of the compound m.p. 105° exhibited bands at 3030 w(C═C-H), 1680 s(C=C-C=O) and 1620 s(C=C) cm^{-1}. The NMR spectrum showed a vinylic proton signal at δ 6.4 which was assigned to C_4-H. The methyl protons were observed at δ 0.96, 0.91, 0.83 and 0.7.

On the basis of the above mentioned spectral properties and its comparison with an authentic sample[146] the compound, m.p. 105° was characterized as 6-oxocholest-4-ene (CCXLIII). The probable mechanism for the formation of 6-oxocholest-4-ene (CCXLIII) from the olefin (CCI) by oxymercuration-demercuration has been shown in scheme 18. This mechanism, involving a π-complex finds support from a similar mechanism suggested by Strini, et al.[140] for the formation of α,β-unsaturated ketones from olefins.

Scheme 18



Characterization of the compound K-1 as 6-oxocholest-4-en-3β-7α-yl diacetate (CCXLIV)

The compound K-1 analysed for $C_{31}H_{48}O_5$. It is evident from the analysis that the compound has gone beyond normal oxymercuration-demercuration.

The IR spectrum of the compound K-1 exhibited the presence of two acetate functions in addition to that of an α,β-unsaturated carbonyl moiety. The spectrum showed absorption band at 3060 (w) which indicated the presence of C=C-H function in the compound. A broad strong band at 1740 cm^{-1} was indicative of the presence of two acetate carbonyl functions in the molecule. The presence of an α,β-unsaturated moiety in the compound was confirmed by yet another strong band at 1680 cm^{-1} and a medium band at 1635 cm^{-1}. The presence of acetate function was further proved by the presence of two broad medium bands at 1240 and 1020 cm^{-1}.

The NMR spectrum of the compound K-1 showed a vinylic proton signal at δ 5.56 which was assigned to the C_4-H. A broad singlet at δ 5.2 was due to the $C_7\beta$-H while a broad multiplet at δ 5.1 was assigned to the $C_3\alpha$ H($W\frac{1}{2}$ = 16 Hz). The presence of two acetate functions in the compound was indicated by the appearance of two acetate methyl proton signals at δ 2.03 and 2.1. The other methyl signals were observed at δ 0.95, 0.81, 0.73 and 0.7.

On the basis of the above spectral properties the compound K-1 was tentatively identified as 6-oxocholest-4-en-3β,7α-yl diacetate (CCXLIV).

Characterization of the compound K-2 as 7-oxocholest-5-en-4α-yl acetate (CCXLV)

The compound K-2 analysed for $C_{29}H_{46}O_3$. The IR spectrum of the compound exhibited a weak band at 3030 cm^{-1} for C=C-H stretching, a strong band at 1740 cm^{-1} for the acetate carbonyl function and a strong and a medium bands at 1670 and 1610 cm^{-1} indicating the presence of -C=C-C=O and C=C, respectively.

The NMR spectrum of the compound exhibited a vinylic proton signal at δ 6.03 which was assigned to the C_6-H. A multiplet ($W\frac{1}{2}$ = 9 Hz) at δ 5.2 was ascribed to the $C_4\beta$-H. The half band width of the signal for C_4-H was indicative of the fact that the acetate function at C_4 was α-oriented. A singlet integrating for three protons at δ 1.97 was due to the acetate methyl protons while the other methyl protons appeared at δ 0.9, 0.83, 0.75 and 0.7.

The compound K-2, on the basis of the above mentioned spectral properties was tentatively identified as 7-oxocholest-5-en-4α-yl acetate (CCXLV).

Characterization of the compound K-3 as 6-oxocholest-4-en-7α-yl acetate (CCXLVI)

The compound K-3 analysed for $C_{29}H_{46}O_3$. The IR spectrum of the compound K-3 showed a strong absorption band at 1735 cm^{-1} which was due to the carbonyl group absorption of the acetate function. A strong band at 1680 (C=C-C=O) and a medium band at 1620 cm^{-1} (C=C) indicated the presence of an α,β-unsaturated carbonyl function in the compound. The bands at 1235 and 1030 cm^{-1} further supported the presence of acetate function.

The NMR spectrum of the compound K-3 exhibited a vinylic proton signal at δ 5.8 which was ascribed to the C_4-H. A broad singlet at δ 5.35 was assigned to the $C_7\beta$-H. A singlet at δ 2.0 integrating for three protons was due to the acetate methyl protons while the other methyl protons appeared at δ 0.93, 0.83, 0.75 and 0.68.

Thus on the basis of the above mentioned spectral data the compound K-3 was tentatively characterized as 6-oxocholest-4-en-7α-yl acetate (CCXLVI).

Characterization of the compound K-4 as 7-oxocholest-4-en-6β-ol-3β-yl acetate (CCXLVII)

The compound K-4 analysed for $C_{29}H_{46}O_4$. The IR spectrum of the compound exhibited absorption bands at 3420 m(OH), 3030 w(C=C-H), 1735 s(CH_3-$\overset{O}{\overset{\|}{C}}$-O), 1715 s(C=O), 1610 w(C=C), 1240

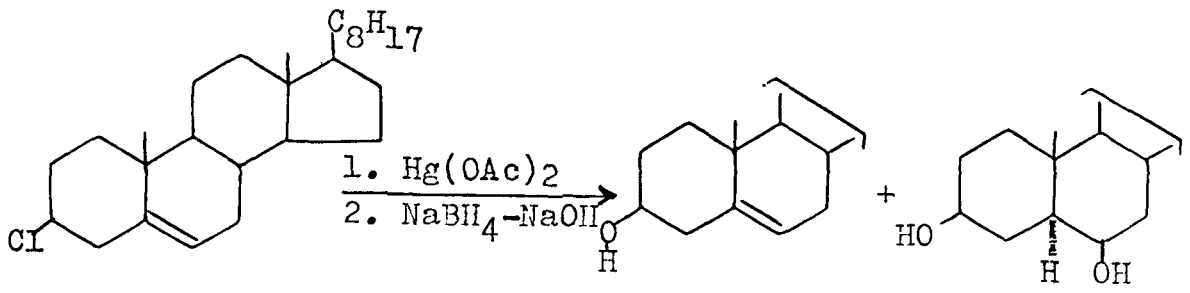
m(acetate) and 1030 m(C-O-).

The NMR spectrum of the compound K-4 showed a vinylic proton signal at δ 5.56 which was assigned to the C_4-H. A broad multiplet at δ 5.01 ($W\frac{1}{2}$ = 14 Hz) was due to the $C_3\alpha$H. The $C_6\alpha$-H appeared at δ 4.15 ($W\frac{1}{2}$ = 5 Hz) as a multiplet. The half-band width of the signal for the C_6-H indicated that the hydroxy group at C_6 was β-oriented (axial). The acetate methyl protons were observed at δ 1.95 as a singlet while the other methyl protons appeared at δ 1.1, 0.89, 0.81 and 0.71.

The compound K-4 on the basis of the foregoing discussion was characterized as 7-oxocholest-4-en-6β-ol-3β-yl acetate (CCXLVII).

Oxymercuration-demercuration of cholest-5-en-3β-yl chloride (CCXXXII) using $Hg(OAc)_2$-$NaBH_4$-NaOH

Oxymercuration of cholest-5-en-3β-yl chloride (CCXXXII) with mercuric acetate in acetic acid gave the organomercury acetate adduct which on demercuration with sodium borohydride in sodium hydroxide solution afforded, after usual work up and chromatography over silica gel, two compounds. One of the compounds was a solid having m.p. 150°, while the other one was a non-crystallizable oil (K-5).



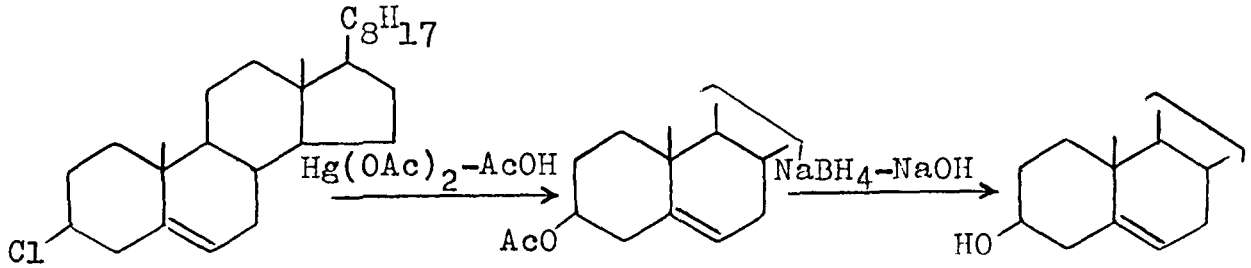
(CCXXXII) (CCXXXVII) (CCXLVIII)

Characterization of the compound m.p. 150° as cholest-5-en-3β-ol (CCXXXVII)

The compound m.p. 150° analysed for $C_{27}H_{46}O$. The compound was identified to be cholest-5-en-3β-ol (CCXXXVII) on the basis of its spectral properties [$\nu_{max.}$ 3380 m(OH), 1620 m(C=C) and 1040 m(C-O) cm^{-1}; δ 5.6 m(C_6-vinylic H), 3.7 m($C_3\alpha$-H, $W\frac{1}{2}$ = 17 Hz), 0.9, 0.81, 0.73 and 0.68 (methyl protons)]. The compound was found to be identical in all respects with an authentic sample of cholesterol[147].

To rationalize the formation of cholest-5-en-3β-ol (CCXXXVII) from cholest-5-en-3β-yl chloride (CCXXXII), it was thought worthwhile to carry out the simple alkaline hydrolysis of (CCXXXII) in order to check whether oxymercuration has played any role in this transformation or not. The hydrolysis of (CCXXXII) at room temperature, however, failed to furnish cholesterol

(CCXXXVII). It was therefore, concluded that during oxymercuration reaction by mercuric acetate and acetic acid, the chlorine at C_3 was substituted by an acetoxy group with the retention of configuration, which on demercuration in sodium hydroxide was hydrolysed to the hydroxy group. The double bond of the olefin (CCXXXII), it seems, remained unaffected during the course of oxymercuration-demercuration reaction.



(CCXXXII) (CCX) (CCXXXVII)

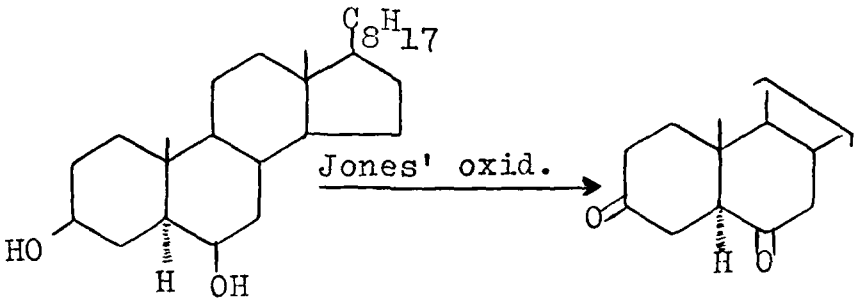
Characterization of the compound K-5 as 5α-cholestane-3β-6β-diol (CCXLVIII)

The compound K-5 analysed for $C_{27}H_{48}O_2$. The IR spectrum of the compound exhibited a broad band at 3460-3380 cm^{-1}, indicating the presence of OH group. There was no other significant band in the IR spectrum.

The NMR spectrum of the compound showed a broad multiplet at δ 3.7, integrating for two protons, which was assigned to $C_3\alpha$-H

and $C_6\alpha$-H. The methyl proton signals appeared at δ 0.91, 0.83, 0.71 and 0.68. On the basis of these spectral properties, the compound K-5 was characterized as 5α-cholestane-3β,6β-diol (CCXLVIII).

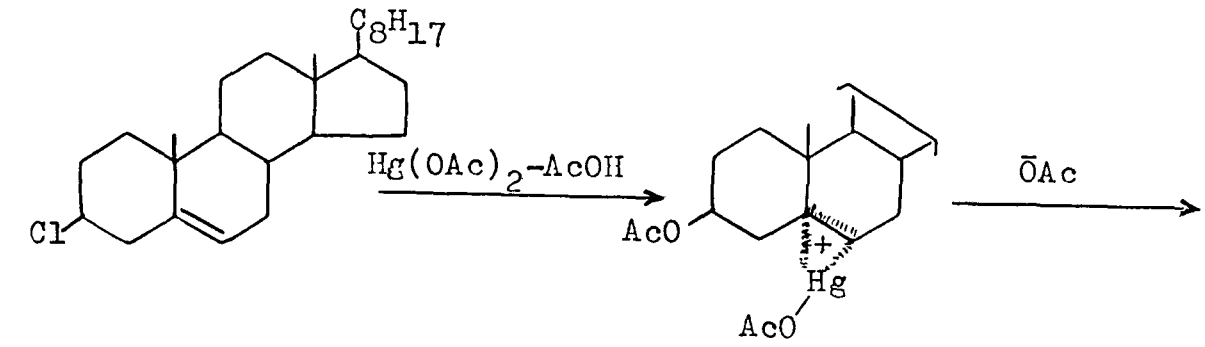
The structure of the compound was chemically justified on the basis of its Jones' oxidation which furnished 3,6-dioxo-5α-cholestane (CXCV). The diketone was found to be identical in all respect (m.p., m.m.p., tlc, co-tlc and spectral properties) with an authentic sample[119].



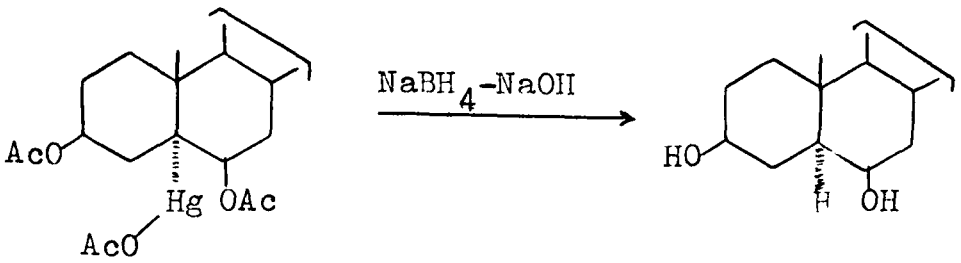
(CCXLVIII) (CXCV)

The probable pathway involved in the formation of diol (CCXLVIII) from the olefin (CCXXXII) can be shown according to scheme 19.

Scheme 19



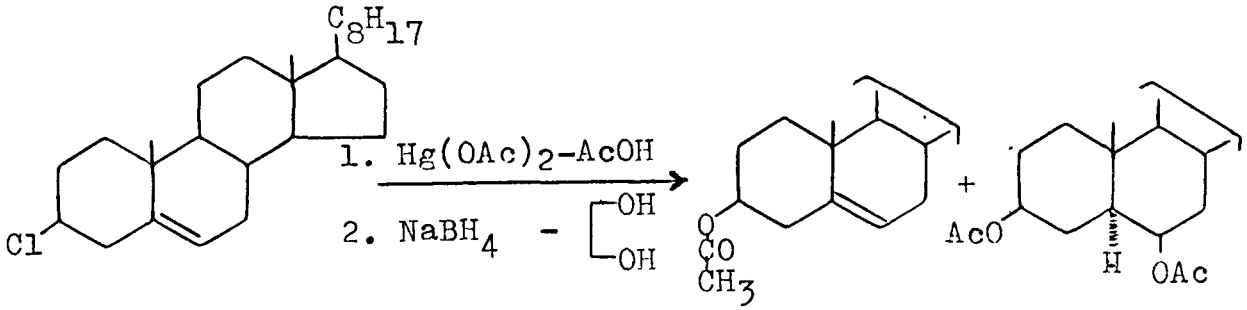
(CCXXXII)



(CCXLVIII)

Oxymercuration-demercuration of cholest-5-en-3β-yl chloride (CCXXXII) with $Hg(OAc)_2$-$NaBH_4$-Ethylene Glycol

Cholest-5-en-3β-yl chloride (CCXXXII) on treatment with mercuric acetate in acetic acid gave the organomercury acetate adduct which on demercuration with sodium borohydride in ethylene glycol furnished two compounds. One of these compounds was a solid having m.p. 115° and the other one was obtained as a non-crystallizable oil (K-6).



(CCXXXII) (CCX) (CCXLIX)

Characterization of the compound m.p. 115° as cholest-5-en-3β-yl acetate (CCX)

The compound m.p. 115° was characterized as cholest-5-en-3β-yl acetate (CCX) on the basis of its spectral properties and comparison with an authentic sample[121].

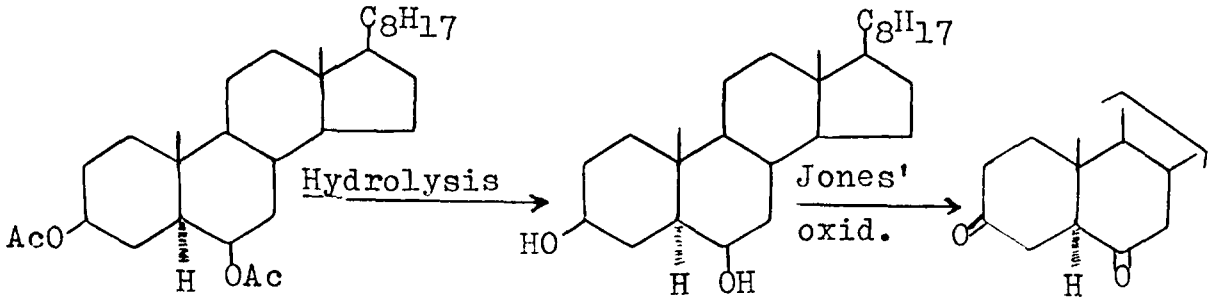
The formation of acetate (CCX) from (CCXXXII) was rationalized on the basis of the fact that during oxymercuration, the chlorine at C_3 is substituted by an acetate function in the presence of mercuric acetate and acetic acid. The carbon-carbon double bond, it seems remained unaffected during the course of the reaction.

Characterization of the compound K-6 as 5α-cholestane-3β-6β-diol diacetate (CCXLIX)

The compound K-6 analysed for $C_{31}H_{52}O_4$. It is evident from the analysis that two acetate functions are present in the compound.

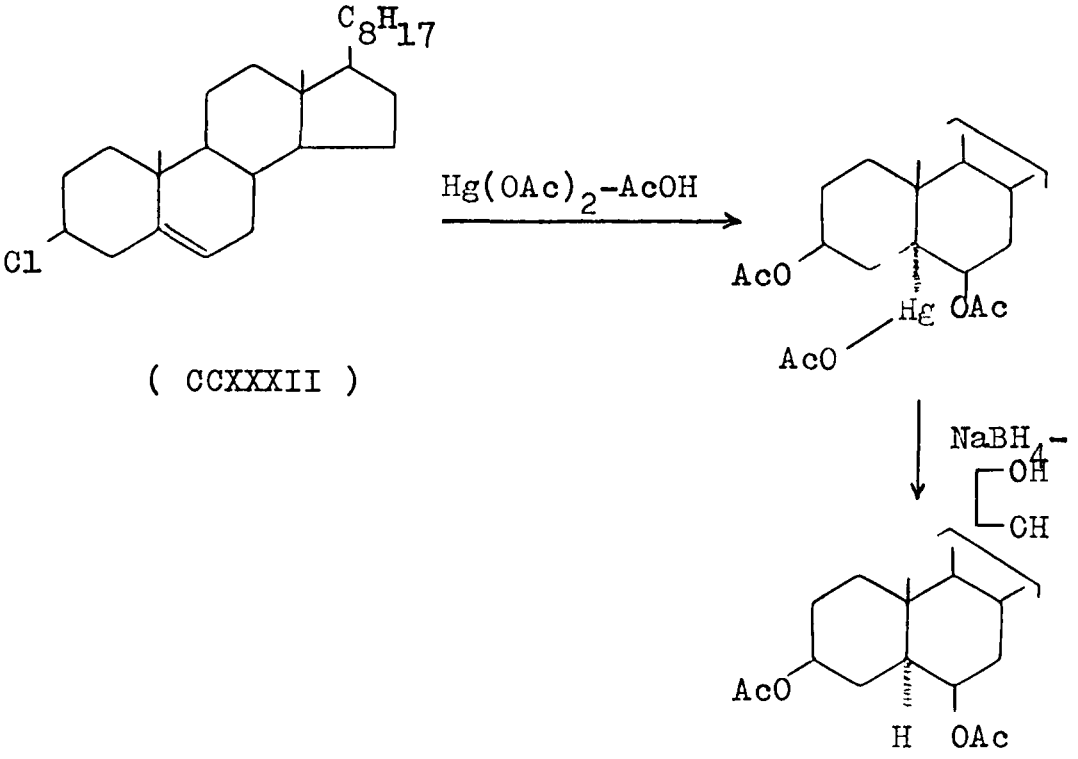
The IR spectrum of the compound showed a strong broad band at 1730-1740 cm^{-1} showing the presence of two acetate carbonyl groups in the compound. The medium bands at 1240 and 1030 cm^{-1} also supported the acetate function. The NMR spectrum of the compound exhibited a broad multiplet at δ 4.6-4.7, integrating for two protons, which was assigned to $C_3\alpha$-H and $C_6\alpha$-H. The acetate methyl protons were observed at δ 2.01 and 2.1 as sharp singlets while the other methyl protons appeared at δ 0.93, 0.8, 0.73 and 0.68.

The structure (CCXLIX) for the compound K-6 was chemically justified on the basis of its hydrolysis which furnished 5α-cholestane-3β,6β-diol (CCXLVIII). The diol on Jones' oxidation furnished 3,6-dioxo-5α-cholestane (CXCV) which was found to be identical in all respects with an authentic sample of the diketone[119].



(CCXLIX) (CCXLVIII) (CXCV)

The formation of the diacetate (CCXLIX) from (CCXXXII) during oxymercuration-demercuration can be accounted for by involving electrophilic substitution of chlorine by an acetoxy group at C_3 and oxymercuration of the C_5-C_6 double bond as the first step. The second step is a simple demercuration reaction wherein the mercuryacetate group at C_5 is replaced by a hydrogen atom. The two acetate functions at C_3 and C_6 survive as no sodium hydroxide was added in the demercuration step.

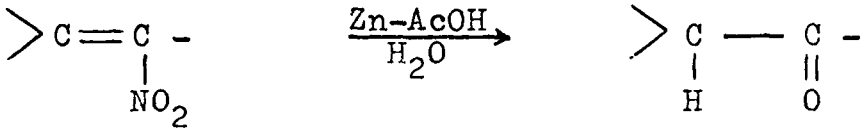


(CCXXXII)

(CCXLIX)

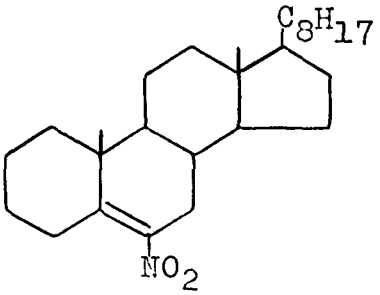
B. REDUCTION OF STEROIDAL NITROOLEFINS WITH Zn-AcOH WITHOUT ADDED WATER

The conversion of vinyl nitro compound into a ketone can be conveniently achieved by Zn-acetic acid-water reduction[148].

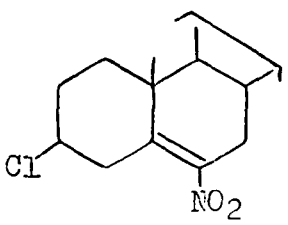


Several intermediates have been postulated in the above conversion and these include imine, amine and oxime[149-151]. It has been claimed that oxime or imine is the precursor of ketone, the later undergoing hydrolytic cleavage[149,150].

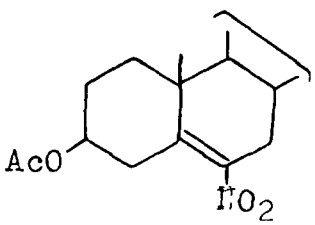
It was considered interesting to conduct the above reaction in the absence of added water and to screen the intermediates. With this purpose in mind we have carried out the reduction of 6-nitrocholest-5-ene (CCL), 6-nitrocholest-5-en-3β-yl chloride (CCLV) and 6-nitrocholest-5-en-3β-yl acetate (CXLVIII) with zinc-acetic acid under non-hydrolytic conditions.



(CCL)



(CCLV)

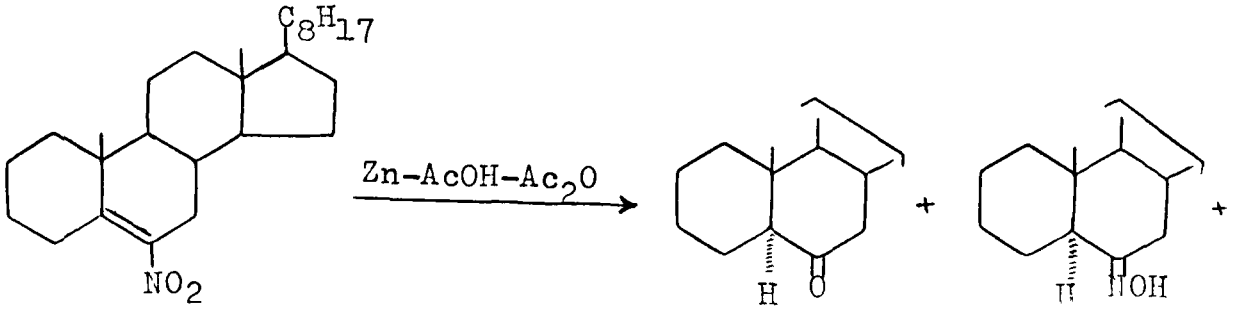


(CXLVIII)

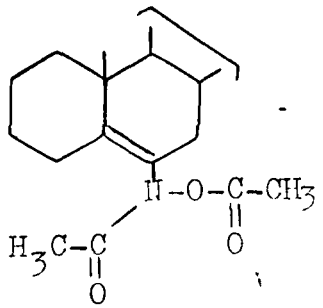
Reduction of 6-nitrocholest-5-ene (CCL) with zinc-acetic acid without added water

6-Nitrocholest-5-ene (CCL) was prepared according to the method described in literature[152].

The reduction of the nitroolefin (CCL) with zinc acetic acid under non-hydrolytic conditions afforded after usual work up and column chromatography over silica gel three different compounds. Two of these had the m.pts.96° and 200° while the third one was obtained as a non-crystallizable oil.



(CCL) (CLXIV) (CLXII)



(CCLI)

Characterization of the compound m.p. 96° as 6-oxo-5α-cholestane (CLXIV)

The compound m.p. 96° was characterized as 6-oxo-5α-cholestane (CLXIV) on the basis of its spectral properties and its comparison with an authentic sample[100]. The formation of the ketone (CLXIV) under non-hydrolytic reaction conditions could be attributed to the traces of moisture that might have come from the atmosphere.

Characterization of the compound m.p. 200° as 6-oximino-5α-cholestane (CLXII)

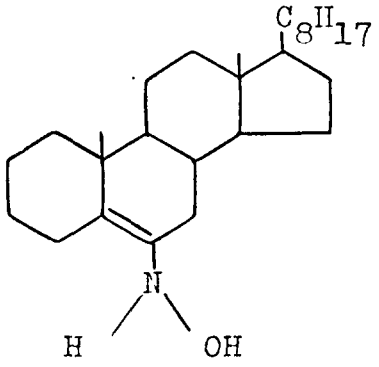
The compound m.p. 200° was identified to be 6-oximino-5α-cholestane (CLXII) on the basis of its spectral properties and comparison with an authentic sample of the oxime[99].

Characterization of the oil as N-acetyl-N-acetyloxy-6-amino-cholest-5-ene (CCLI)

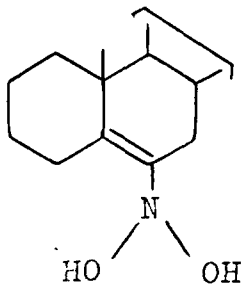
The non-crystallizable oil, obtained on reduction of the nitroolefin (CCL), analysed for $C_{31}H_{51}NO_3$.

The IR spectrum of the oil exhibited two strong carbonyl bands at 1710 and 1670 cm^{-1}, indicating thereby the presence of O-CO-CH_3 and HN-CO-CH_3 groups, respectively. A strong band between 1230-1250 cm^{-1} further supported the presence of acetate function. The absence of any N-H absorption in the IR spectrum

and the presence of two carbonyl functions was indicative of the fact that the intermediate formed as a result of reduction of the nitro group could be either (CCLII) or (CCLIII).



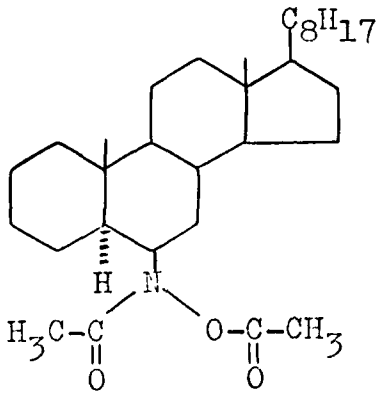
(CCLII)



(CCLIII)

Both the structures (CCLII) and (CCLIII) are capable of reacting with acetic acid twice. The analysis of the dicarbonyl compound however, suggests the intermediacy of (CCLII) to give (CCLI).

The NMR spectrum of the compound (CCLI) gave two singlets at δ 2.3 (3H) and 2.1 (3H) which can be assigned to two $CH_3C{=}O$ groups. There was no signal from δ 2.3 to δ 10. The other methyl signals were observed at δ 1.1, 0.91, 0.81 and 0.7. The absence of any signal between δ 2.3 downward clearly eliminates the possibility of structure such as (CCLIV).

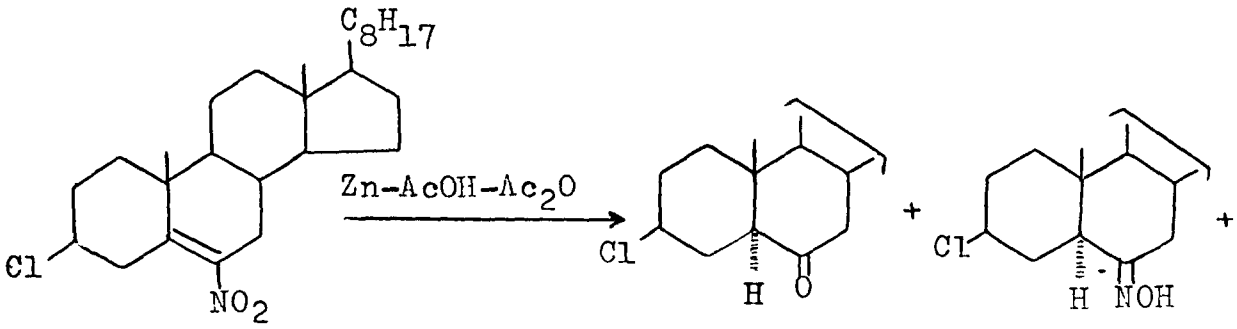


(CCLIV)

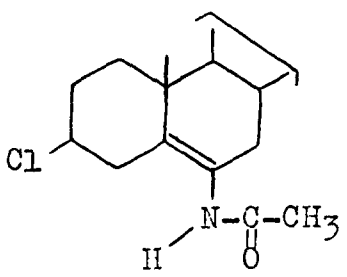
Reduction of 6-nitrocholest-5-en-3β-yl chloride (CCLV) with zinc-acetic acid without added water

6-Nitrocholest-5-en-3β-yl chloride (CCLV) was prepared according to the literature procedure[153].

Reduction of the nitroolefin (CCLV) with zinc-acetic acid in the presence of acetic anhydride furnished after usual work up and column chromatography, three compounds, having m.pts. 128°, 175° and 103°.



(CCLV) (CLXIX) (CLXVII)



(CCLVI)

Characterization of the compound m.p. 128° as 6-oxo-5α-cholestan-3β-yl chloride (CLXIX)

The compound m.p. 128° was characterized as 6-oxo-5α-cholestan-3β-yl chloride (CLXIX) on the basis of its spectral properties and its comparison with an authentic sample of the ketone[102].

Characterization of the compound m.p. 175° as 6-oximino-5α-cholestan-3β-yl chloride (CLXVII)

The compound m.p. 175° was identified to be 6-oximino-5α-cholestan-3β-yl chloride (CLXVII) on the basis of its spectral data and its comparison with an authentic sample of the oxime[101].

Characterization of the compound m.p. 103° as N-acetyl-6-amino-cholest-5-en-3β-yl chloride (CCLVI)

The compound m.p. 103° analysed for $C_{29}H_{48}NOCl$. It gave positive Beilstein test.

The IR spectrum of the compound m.p. 103° was devoid of any band responsible for the nitro group. It showed a band at 3420 cm^{-1} for the N-H stretching. A strong band at 1660 cm^{-1} was due to N-$\underset{\underset{O}{\|}}{C}$-$CH_3$ stretching frequency while a weak band at 1620 cm^{-1} indicated the presence of C=C. A medium band at 750 cm^{-1} was due to C-Cl stretching.

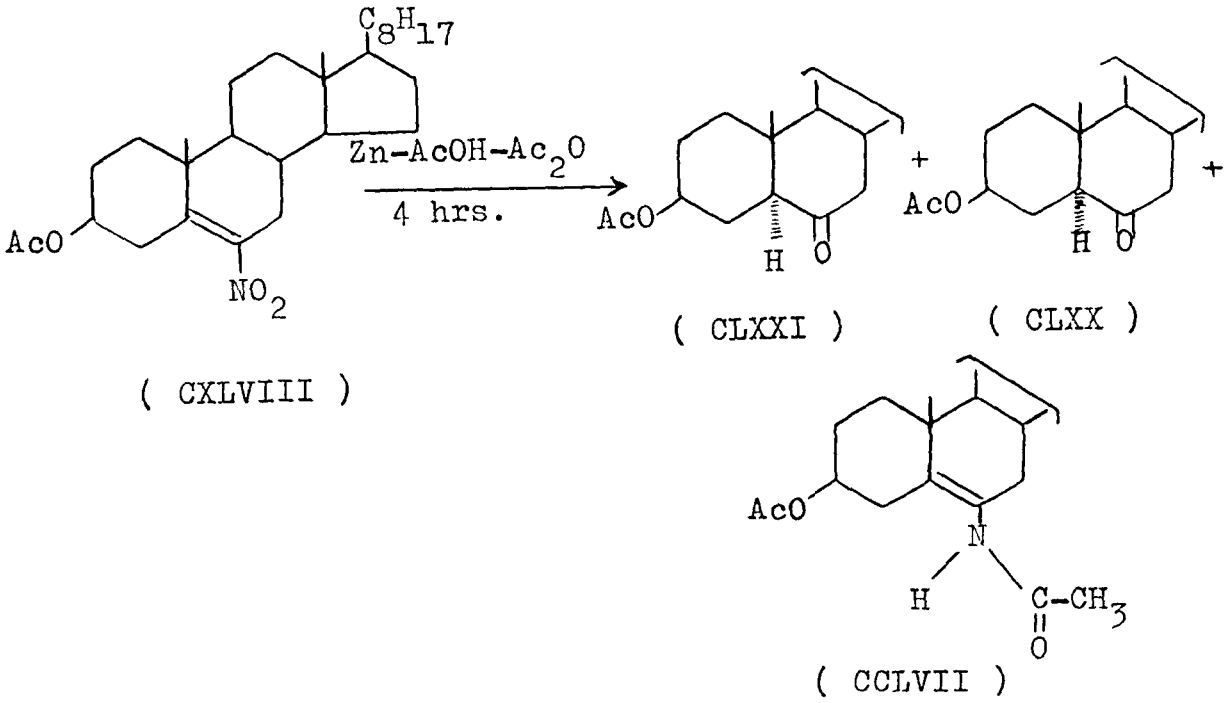
The NMR spectrum of the compound exhibited a broad signal at δ 8.6 for the amine proton. A broad multiplet at δ 3.7 was assigned to the $C_3\alpha$-H ($W\frac{1}{2}$ = 16 Hz). A sharp singlet integrating for three protons at δ 2.01 was due to $C\underline{H}_3CON$ while the other methyl protons appeared at δ 1.1, 0.93, 0.81 and 0.7.

On the basis of the above mentioned spectral properties, it was thought that the nitroolefin (CCLV) under the reaction conditions underwent reduction to the amine function which in the presence of acetic anhydride and acetic acid, was N-acylated to give N-acetyl-6-aminocholest-5-en-3β-yl chloride (CCLVI).

Reduction of 6-nitrocholest-5-en-3β-yl acetate (CXLVIII) with zinc-acetic acid-acetic anhydride

6-Nitrocholest-5-en-3β-yl acetate (CXLVIII) was prepared according to the procedure described in literature[121].

Reduction of (CXLVIII) with zinc-acetic acid in the presence of acetic anhydride furnished after usual work up and chromatography over silica gel, three compounds having m.pts. 127°, 200° and 165°.



(CXLVIII) (CLXXI) (CLXX)

(CCLVII)

Characterization of the compound m.p. 127° as 6-oxo-5α-cholestan-3β-yl acetate (CLXXI)

The compound m.p. 127° was characterized as 6-oxo-5α-cholestan-3β-yl acetate (CLXXI) on the basis of its spectral properties and comparison with an authentic sample[104].

Characterization of the compound m.p. 200° as 6-oximino-5α-cholestan-3β-yl acetate (CLXX)

The compound m.p. 200° was identified to be 6-oximino-5α-cholestan-3β-yl acetate (CLXX) on the basis of its spectral data and its comparison with an authentic sample of the oxime[103].

Characterization of the compound m.p. 165° as N-acetyl-6-amino-cholest-5-en-3β-yl acetate (CCLVII)

The compound m.p. 165° analysed for $C_{31}H_{51}NO_3$. The IR spectrum of the compound m.p. 165° exhibited a doublet at 3350-3300 for the N-H stretching frequency. Two strong bands at 1725-1660 cm^{-1} were assigned to the C_3 acetate carbonyl and the amide carbonyl ($NH-CO-CH_3$), respectively. The presence of acetate was further confirmed by the presence of bands at 1240 and 1030 cm^{-1}.

The NMR spectrum of the compound exhibited a broad signal, integrating for one proton, at δ 7.4 which was assigned to the $\underline{NH}-\overset{O}{\overset{\|}{C}}-$. A broad multiplet at δ 4.5 ($W_{\frac{1}{2}}$ = 14 Hz) was due to the $C_3\alpha$-H. The acetyl methyl protons appeared at δ 1.98 and 1.91. ($C\underline{H}_3-\overset{O}{\overset{\|}{C}}-O$, $C\underline{H}_3-\overset{O}{\overset{\|}{C}}-N-$) while the other methyls were observed at δ 1.07, 0.91, 0.83 and 0.7.

On the basis of these spectral properties, the compound m.p. 165° was characterized as N-acetyl-6-aminocholest-5-en-3β-yl acetate (CCLVII).

PART - FOUR

MASS SPECTRAL STUDIES ON STEROIDAL NITRO COMPOUNDS

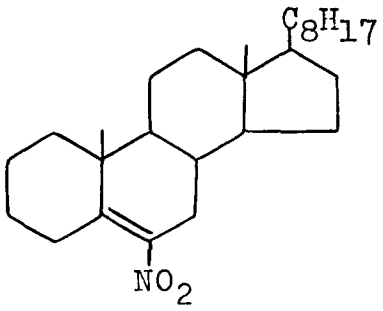
A. C-NITROSTEROIDS

The mass spectral studies on several aliphatic, alicyclic and aromatic nitro compounds[75] have been carried out during the last three decades. These studies have not only served as a tool in assigning the correct structures to these compounds but have also helped in establishing the structure-spectra relationship.

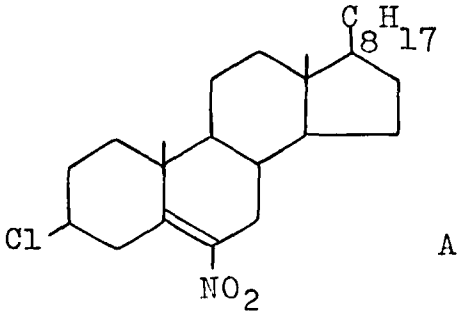
A survey of the literature revealed that β-nitrostyrenes[97] are the only olefinic nitro compounds whose mass spectral studies have been carried out in detail. The mass spectra of these nitrostyrenes are characterized by the fragmentation patterns which are characteristic of both aliphatic as well as aromatic nitro compounds[97]. The presence of a strong molecular ion peak and the loss of nitric oxide from the moelcular ion are reminiscent of aromatic nitro compounds while the resemblance to the aliphatic nitro compounds indicated by the elimination of a nitro group from the molecular ion.

The interesting features of the mass spectra of nitro compounds in general, and that of β-nitrostyrene in particular, prompted us to undertake the mass spectral studies of some of the easily accessible steroidal nitroolefins in the cholestane series,

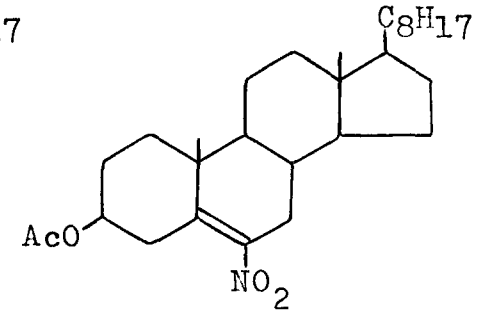
such as 6-nitrocholest-5-ene (CCL), 6-nitrocholest-5-en-3β-yl chloride (CCLV) and 6-nitrocholest-5-en-3β-yl acetate (CXLVIII). These studies were carried out with a view to assess the effect of nitro group and to evaluate the effect of substituents on the fragmentation pattern.



(CCL)



(CCLV)



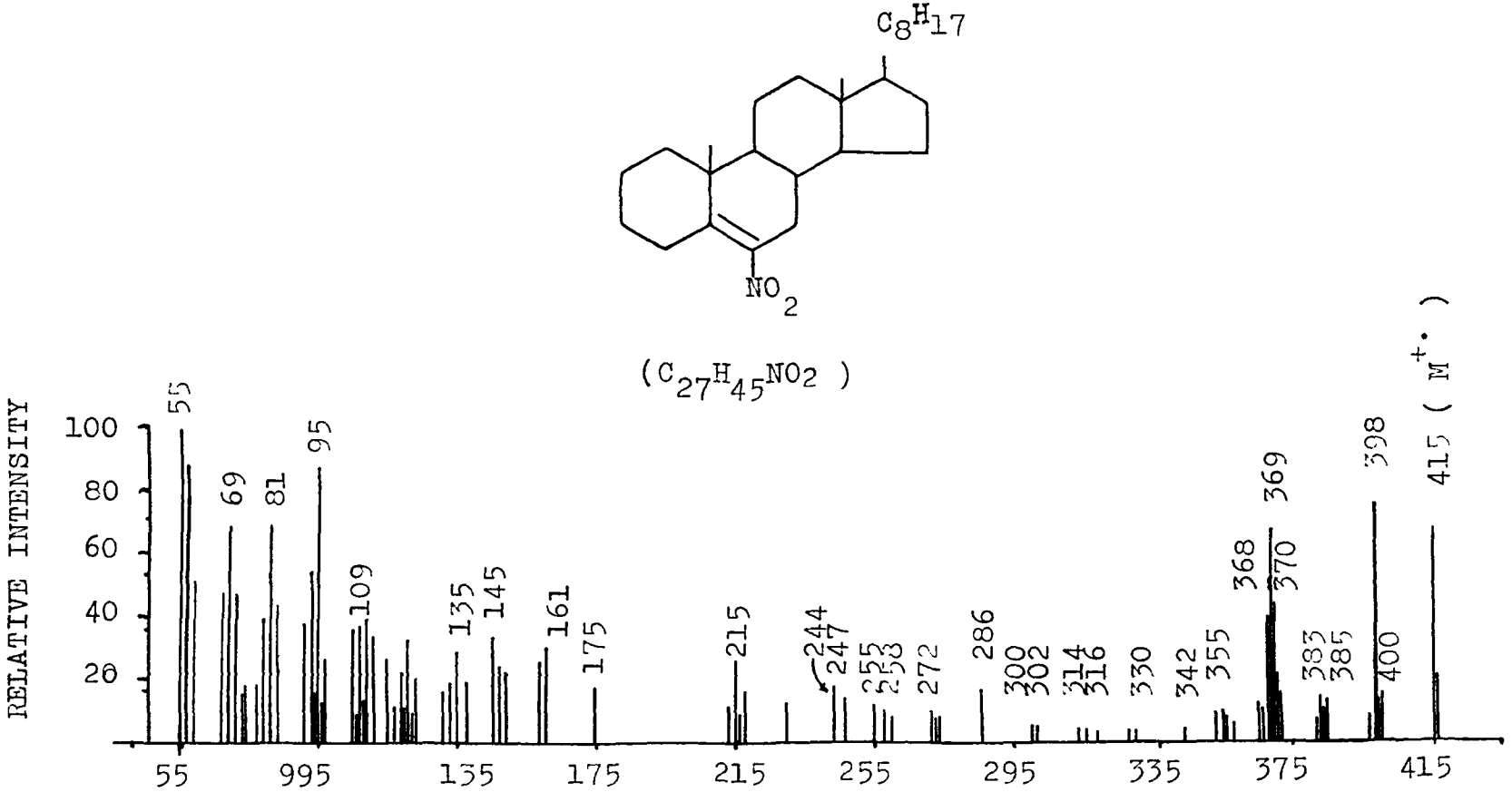
(CXLVIII)

The mass spectrometeric fragmentation pattern of the nitroolefins (CCL), (CCLII) and (CXLVIII) was expected to follow the same course due to their similar structures, offering thereby a means of characterization by mass spectrometry. Only the mass spectrum of 6-nitrocholest-5-ene (CCL) has been discussed in some detail, as this may be considered as the representative model for the nitroolefins and a comparison has been made with (CCLV) and (CXLVIII). The fragmentation pathways suggested in some cases are supported by appropriate metastable peaks. The mechanistic schemes are tentative in the absence of mass spectra of the appropriate deuterated analogues and accurate mass measurements of the fragment ions.

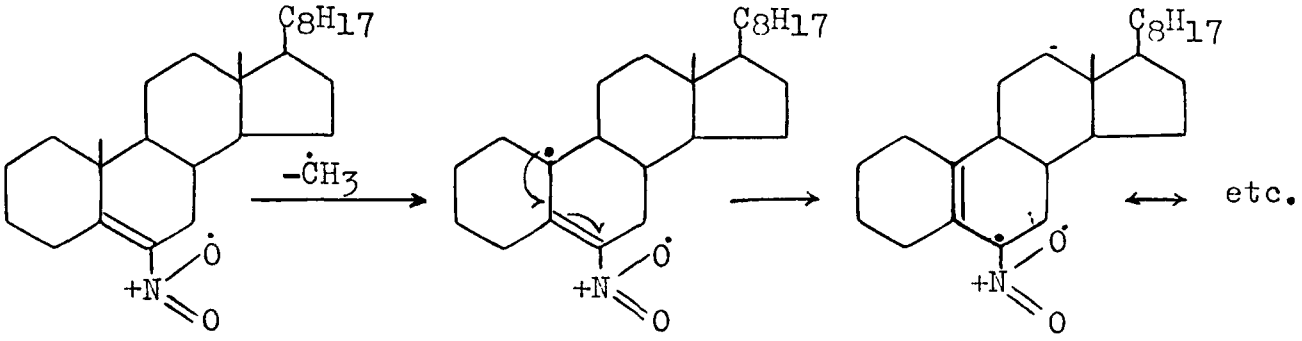
The mass spectrum of 6-nitrocholest-5-ene (CCL) (Figure 1) exhibited the fragment ions which are characteristic of both aliphatic as well as aromatic nitro compounds as does the β-nitrostyrene[97]. The mass spectrum of (CCL) showed a relatively strong molecular ion peak at m/z 415 ($C_{27}H_{45}NO_2$) which was reminiscent of aromatic nitro compounds but not of aliphatic nitro compounds, where the molecular ion peaks are either insignificant or are not observed at all[75]. The molecular ion peak was follwed by the fragment ion peaks at m/z 400, 399, 398, 385, 384, 383, 382, 372, 371, 370, 369, 368, 367, 366, 358, 356, 355, 354, 353, 342, 330, 328, 316, 314, 302, 300, 286, 272, 258, 255, 247, 244, 232, 230, 218, 216, 215, 213, 175, 161, 159, 149, 147, 145 and lower mass peaks. The genesis of some of the significant fragment ions from (CCL) may be explained according to the following schemes.

m/z 400

The ion m/z 400, most probably arises by the loss of a methyl radical, preferentially C_{10}-CH_3, from the molecular ion. In this case the species formed is likely to be stabilized. The transition m/z 415 ⟶ m/z 400 is supported by a metastable peak at m/z 385.5 (Calcd. 385.54).


C_8H_{17}
NO_2
$(C_{27}H_{45}NO_2)$
RELATIVE INTENSITY
100
80
60
40
20
55
69
81
95
109
135
145
161
175
215
244
247
255
272
286
300
302
314
316
330
342
355
368
369
370
383
385
398
400
415 ($M^{+\cdot}$)
55
995
135
175
215
255
295
335
375
415
m/z

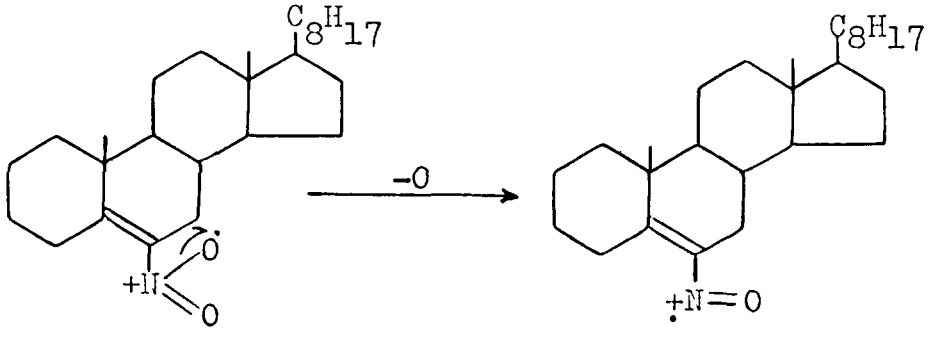
(Figure 1)



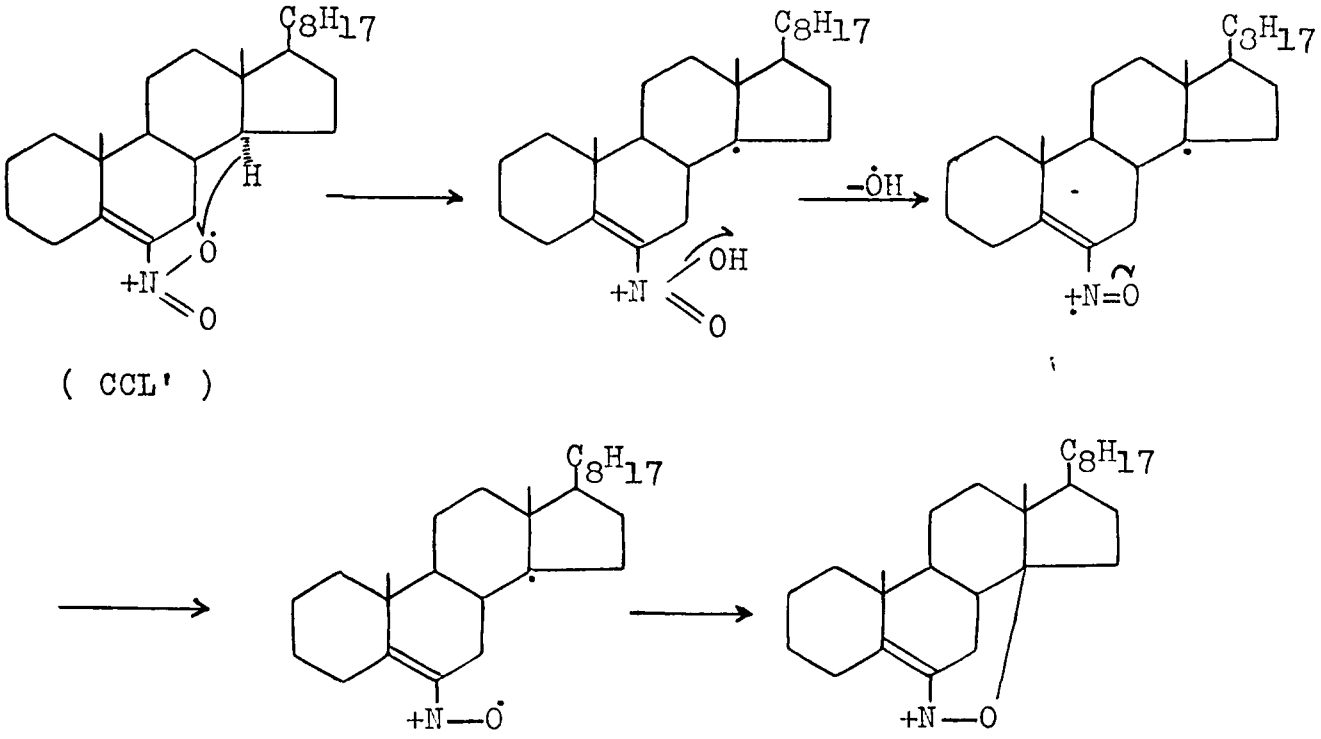
(CCL') m/z 400

m/z 399 and m/z 398

These ions may arise by the loss of an oxygen atom and a hydroxyl radical, respectively, from the molecular ion. The loss of oxygen and hydroxyl radical constitute one of the most frequently observed fragmentation processes in the mass spectrometry of nitro compounds[75]. The two transitions (m/z 415 → m/z 399 and m/z 415 → m/z 398) are supported by metastable peaks observed at 383.6 (Calcd. 383.61) and 381.7 (Calcd. 381.69), respectively.



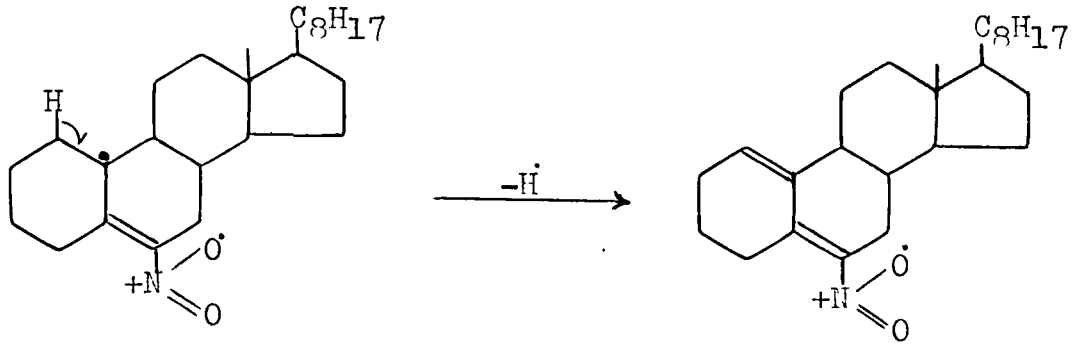
(CCL') m/z 399(a)



(CCL')

m/z 398

Alternatively, the ion m/z 399 can also be shown to arise by the loss of a hydrogen radical from the ion m/z 400. Though no metastable was observed for the transition m/z 400 ⟶ m/z 399, this can not be taken as an evidence against this transition.

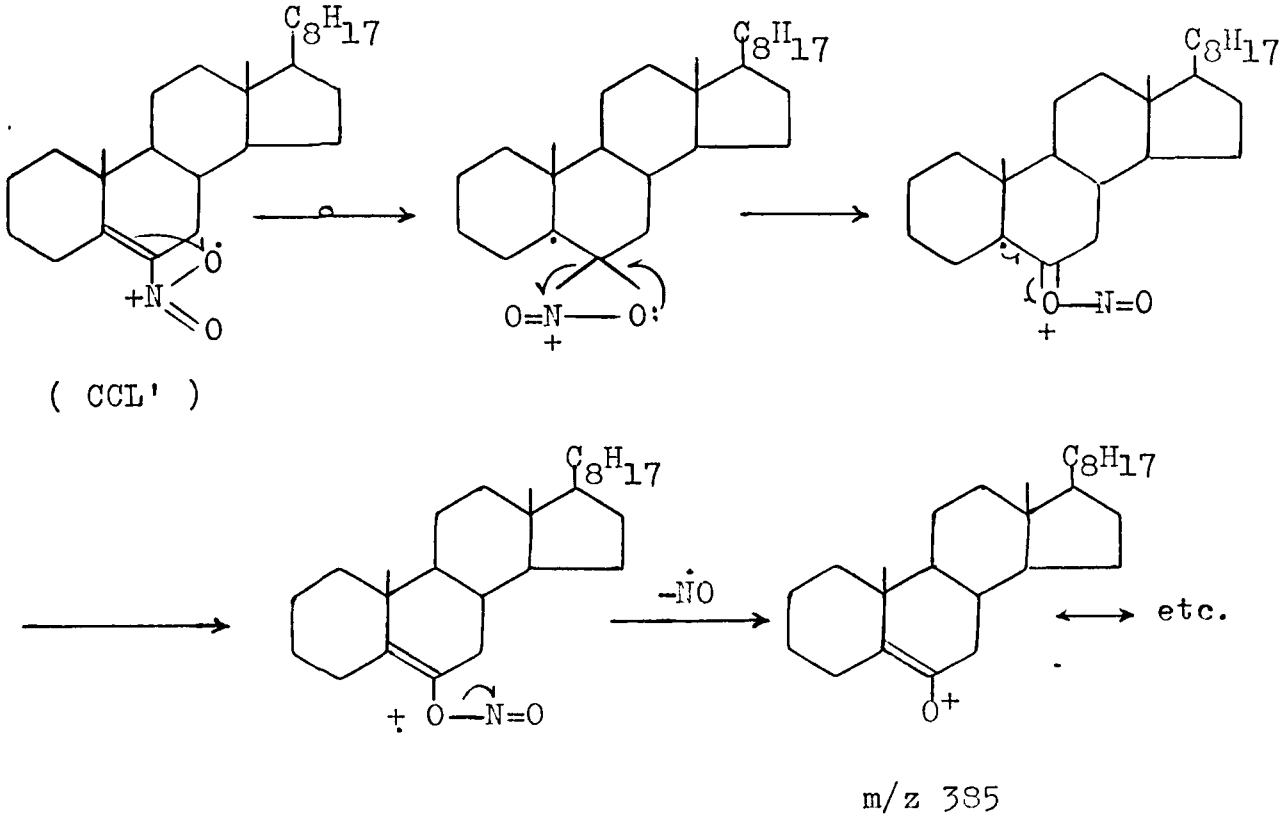


m/z 400

m/z 399 (b)

m/z 385

The fragment ion m/z 385 is most likely formed by the loss of nitric oxide (NO) from the molecular ion. Though the loss of NO from the molecular ion is characteristic of aromatic nitro compounds but the evidence for such a loss from nitroolefins also exists[97]. The loss of nitric oxide from a nitro group has been explained on the basis of its rearrangement to the isomeric nitrite form prior to the fragmentation in a one-step process. It is pertinent to note that the photochemical precedent[96] exists for such a rearrangement. The transition m/z 415 ⟶ m/z 385 finds support by metastable ion at m/z 357.2 (Calcd. 357.16).

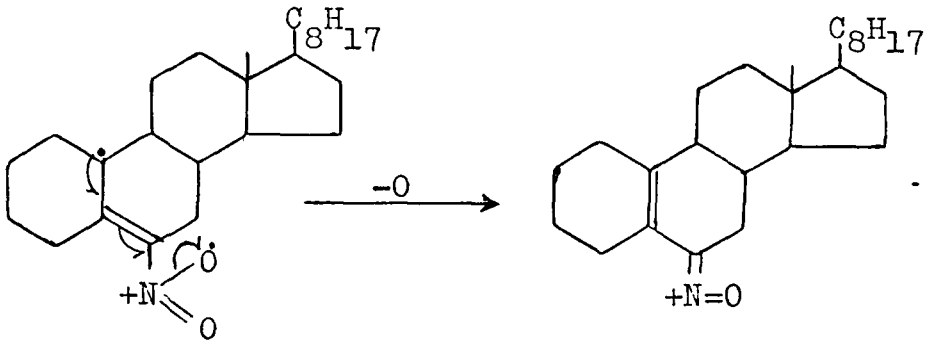


(CCL')

m/z 385

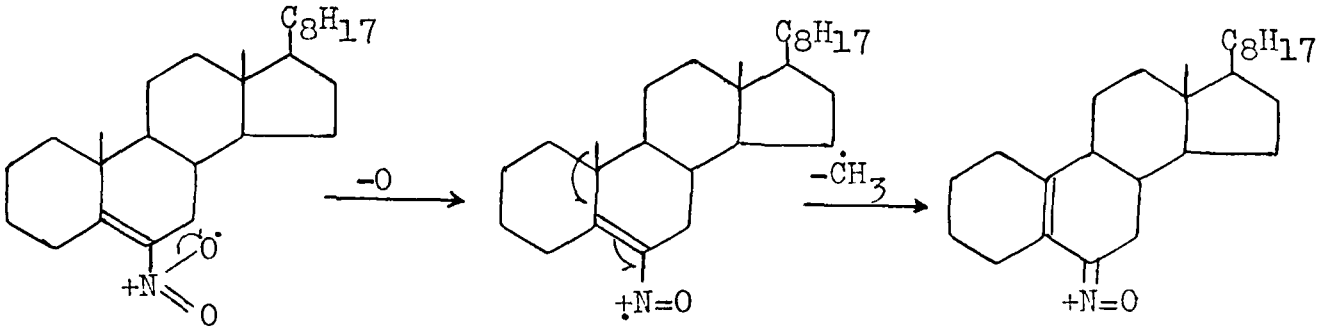
m/z 384

The ion m/z 384 may be shown to arise by the loss of an oxygen atom from the ion m/z 400. Inversely, this ion may also arise by the loss of a methyl radical from the ion m/z 399, formed by the loss of an oxygen atom from the molecular ion.



m/z 400 m/z 384

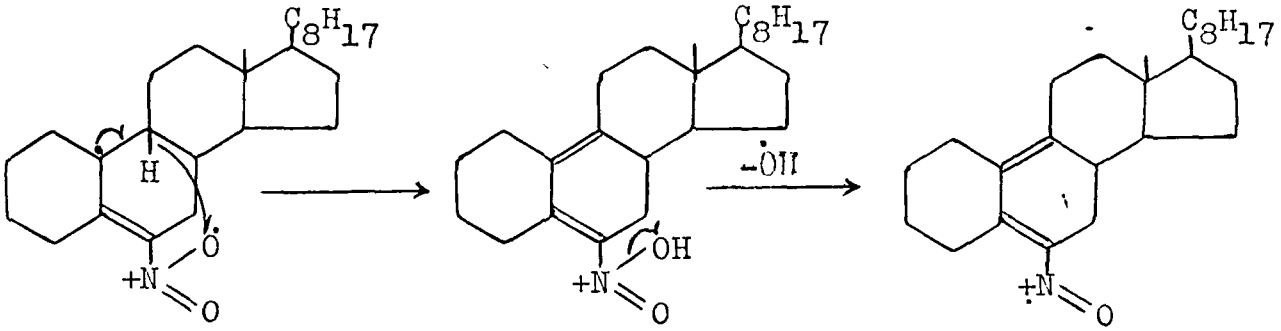
OR



(CCL') m/z 399 m/z 384

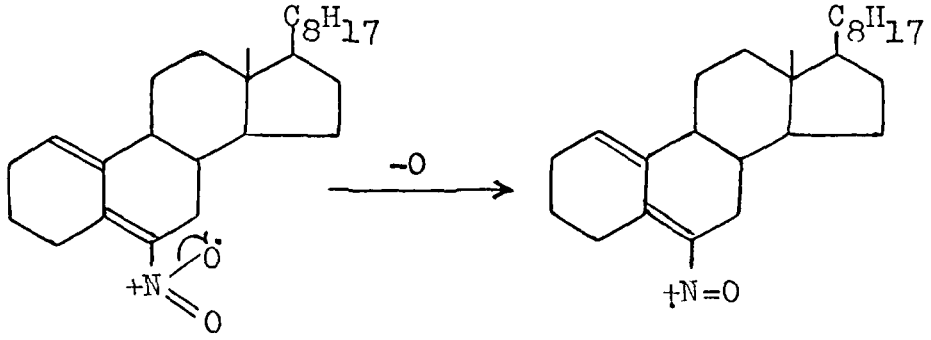
m/z 383

This ion most probably arises by the loss of a hydroxyl radical from the ion m/z 400.



m/z 400 m/z 383

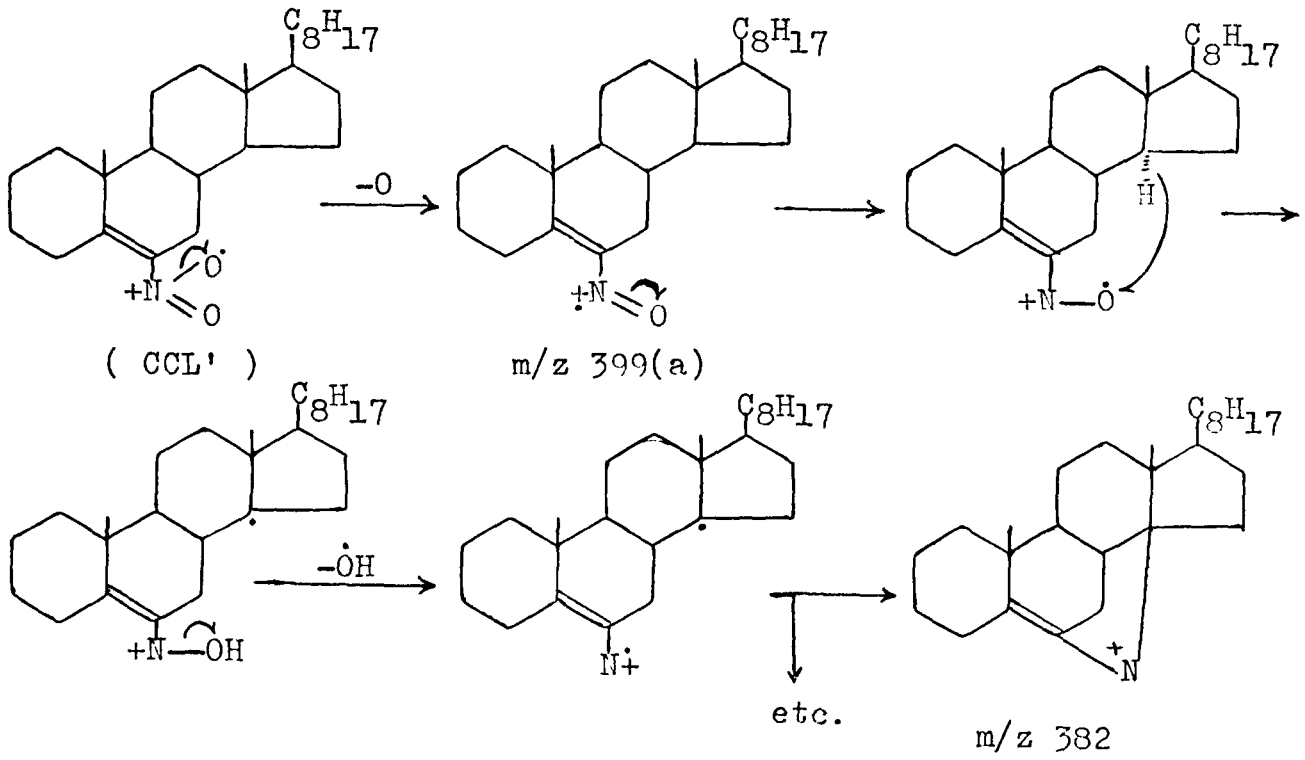
Alternatively, the ion m/z 383 may also arise by the loss of an oxygen atom from the ion m/z 399 (b).



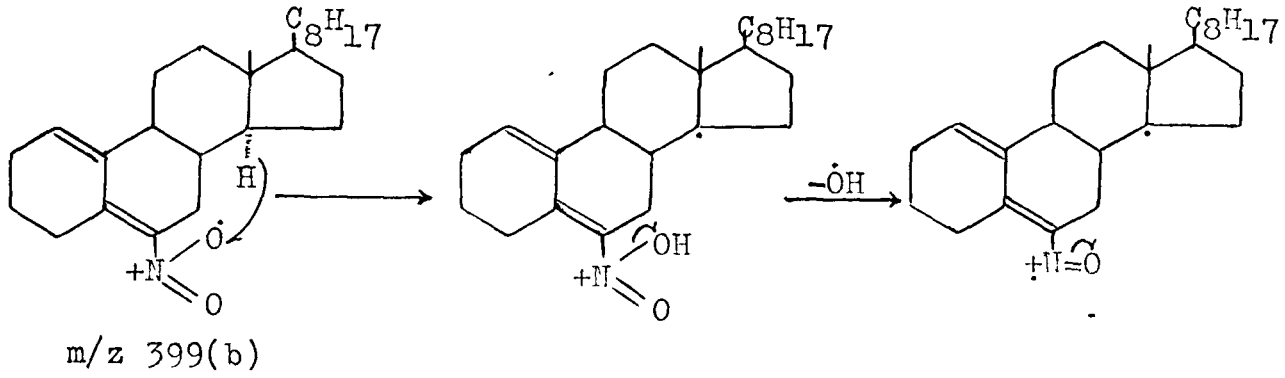
m/z 399(b) m/z 383

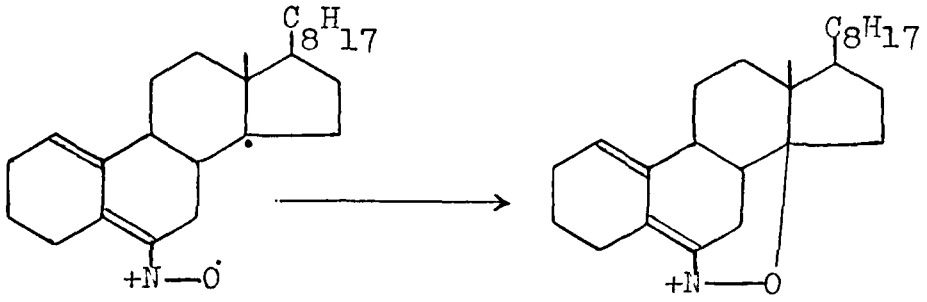
m/z 382

The ion m/z 382 may be shown to arise by the loss of both the oxygen atoms, apparently by the sequential elimination of an oxygen and of a hydroxyl radical.



Alternatively, this ion can also arise from the ion m/z 399 (b) by the loss of a hydroxyl radical.

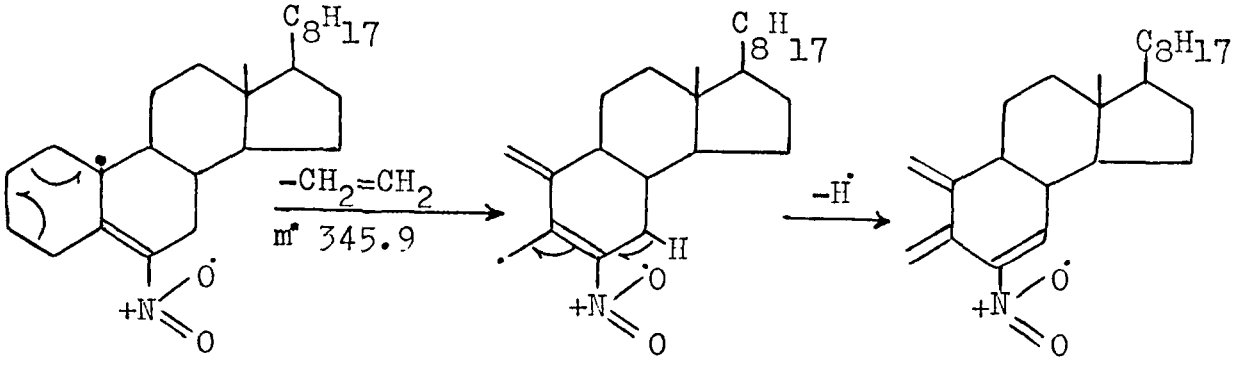




m/z 382

m/z 372 and m/z 371

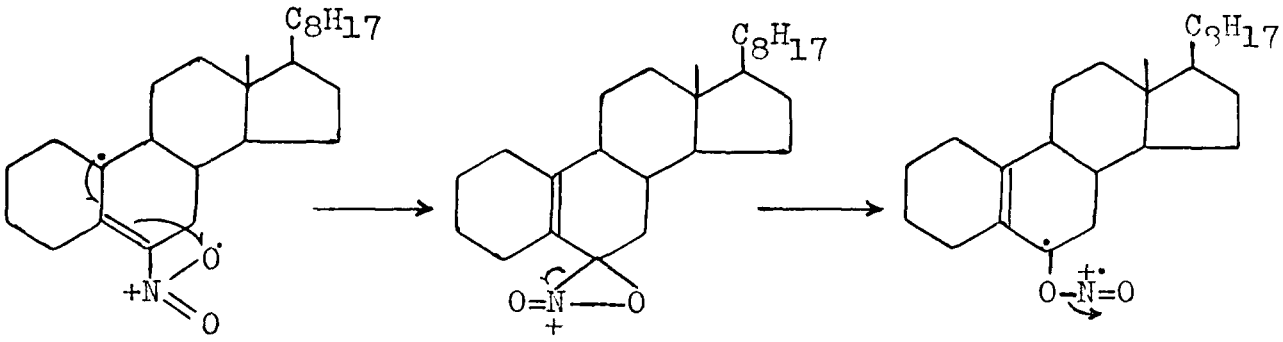
The ion m/z 372 arises from the ion m/z 400, by the loss of ethylene from ring A. Further loss of hydrogen from the ion m/z 372 gives the ion m/z 371.



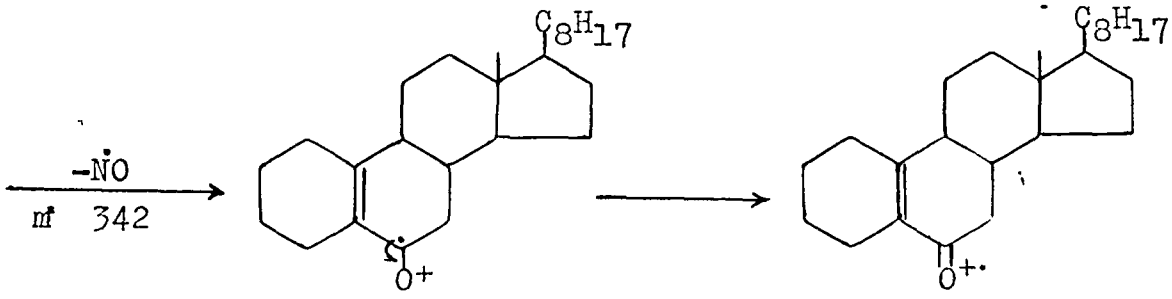
m/z 400 m/z 372 m/z 371

m/z 370

This ion may be accounted for by the loss of nitric oxide from the ion m/z 400. The ion m/z 400, undergoes rearrangement to the isomeric nitrite form which then eliminates nitric oxide to give the ion m/z 370.

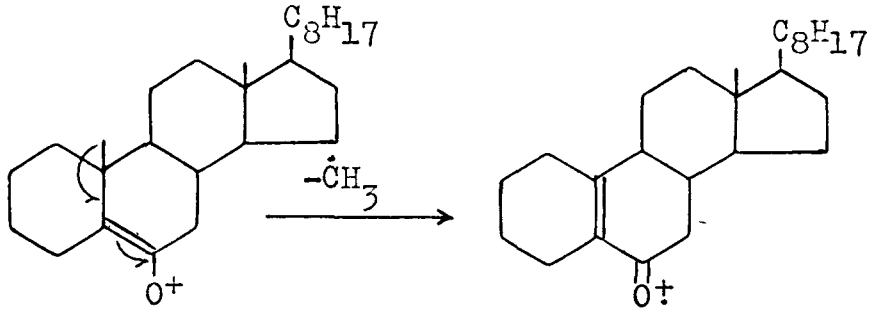


m/z 400



m/z 370

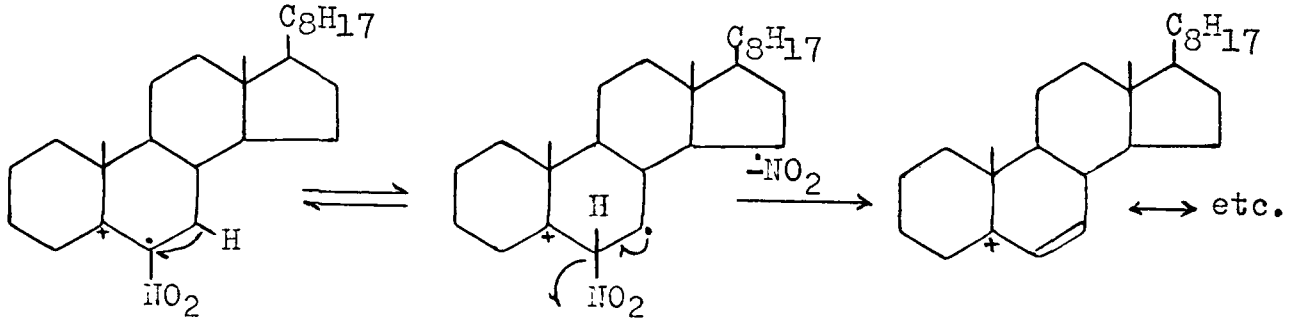
Alternatively, this ion can also arise from the ion m/z 385 by the loss of a methyl radical.



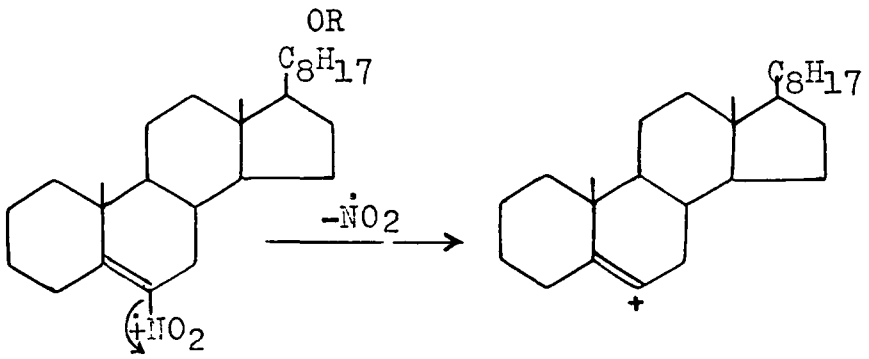
m/z 385 m/z 370

m/z 369 and m/z 368

The ion m/z 369, constituting the base peak in the mass spectrum of (CCL) most probably arises by the loss of NO_2 from the molecular ion. The loss of NO_2 from the molecular ion is one of the most significant fragmentations[75] in the mass spectra of aliphatic and alicyclic nitro compounds and is responsible for the base peak in most of the cases. The ion m/z 368 may arise by the loss of the elements of nitrous acid[73] from the molecular ion. The loss of NO_2 from the molecular ion, by analogy, can be written as in the following scheme.

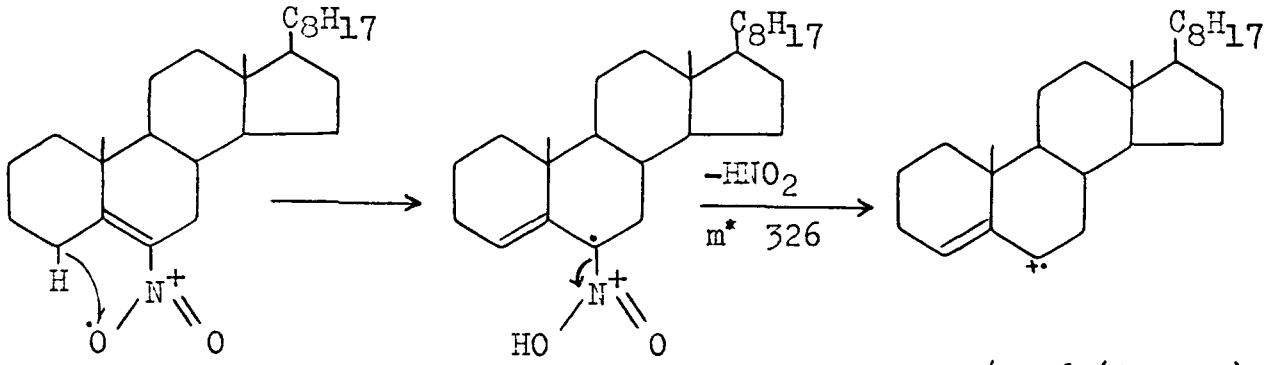


m/z 415 m/z 369($C_{27}H_{45}$)



(CCL') m/z 369

The transition m/z 415 ⟶ m/z 369 finds support from a metastable peak at m/z 328.0 (Calcd. 328.09). There could be other precursor for the ion m/z 369, for example m/z 370 - H. The ion m/z 368 arises from the molecular ion as follows.

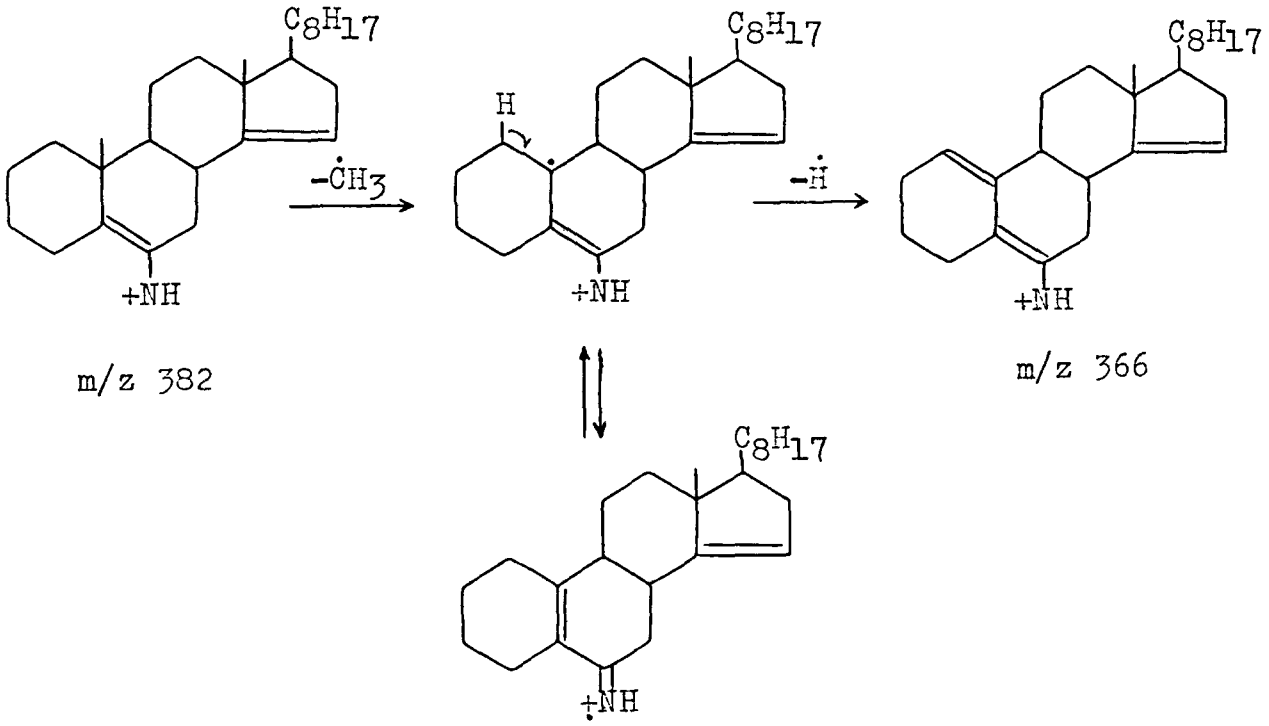


m/z 368($C_{27}H_{44}$)

(CCL')

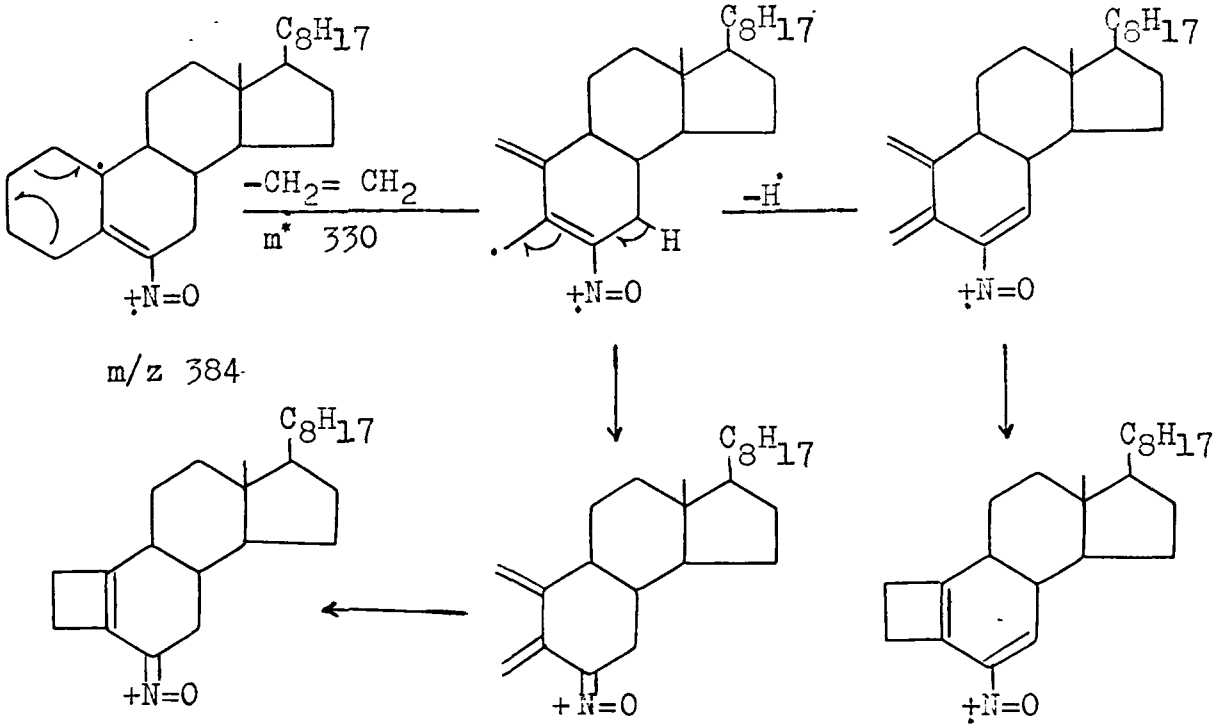
m/z 367 and m/z 366

The ion m/z 367 may be shown to arise by the loss of a methyl radical from the ion m/z 382; subsequent loss of a hydrogen may give the ion m/z 366.

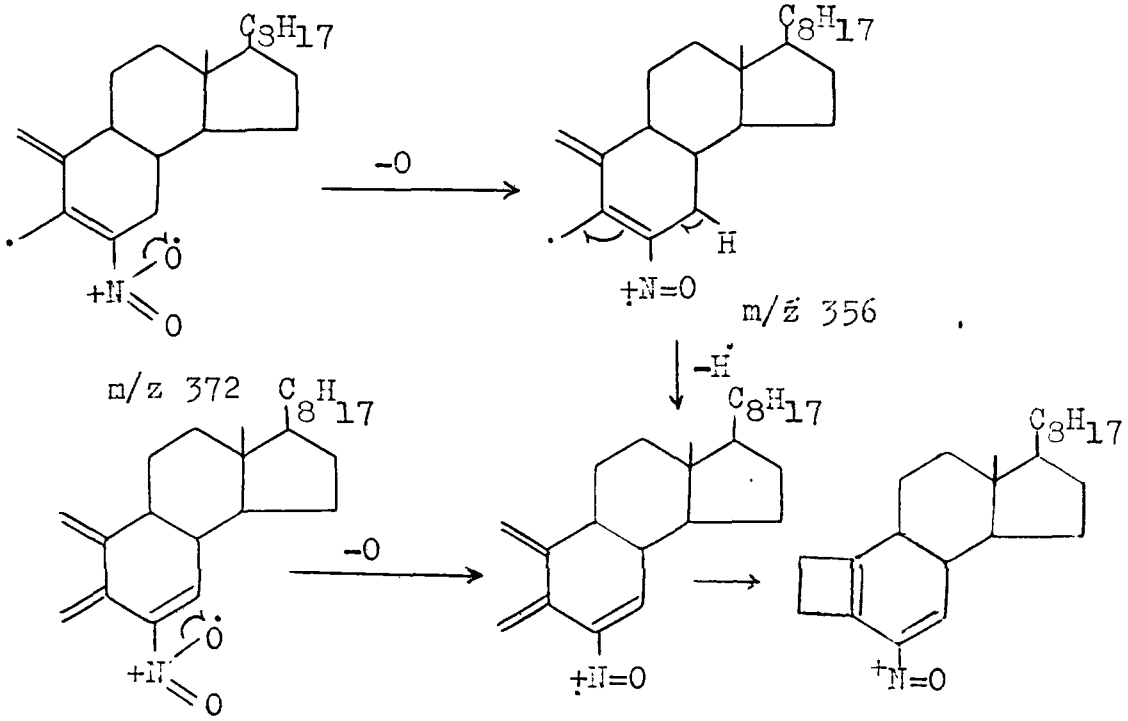


m/z 356 and m/z 355

The ion m/z 356 arises most probably from the ion m/z 384 by the loss of ethylene. The ion m/z 356 may then lose a hydrogen radical to give the ion m/z 355.

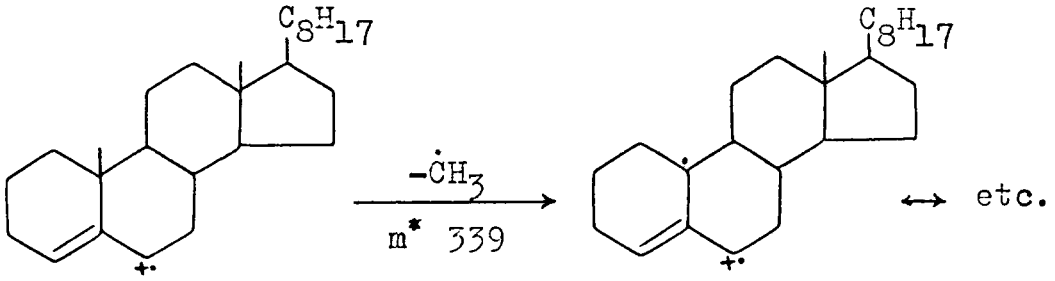


Alternatively, these ions may also arise by the loss of an oxygen atom from the ions m/z 372 and 371, respectively.



m/z 353

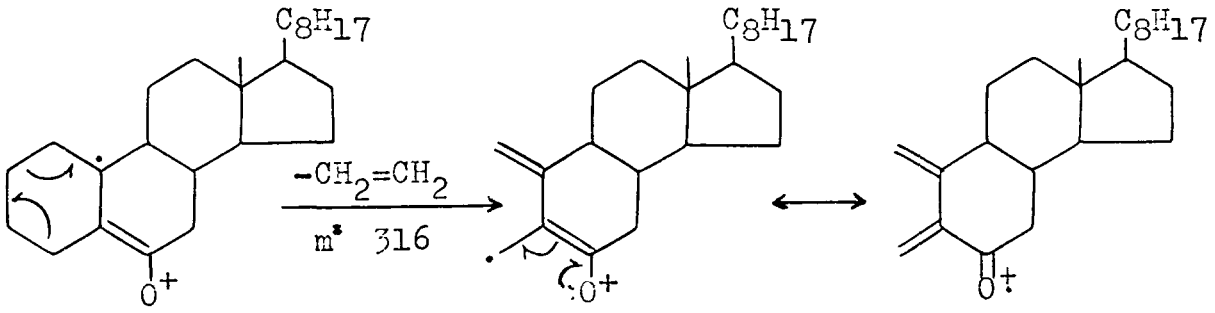
This ion arises most probably by the loss of a methyl radical from the ion m/z 368.



m/z 368($C_{27}H_{44}$) m/z 353

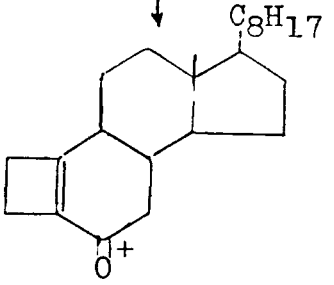
m/z 342

The ion m/z 342 may be shown to arise by the loss of ethylene from the ion m/z 370.



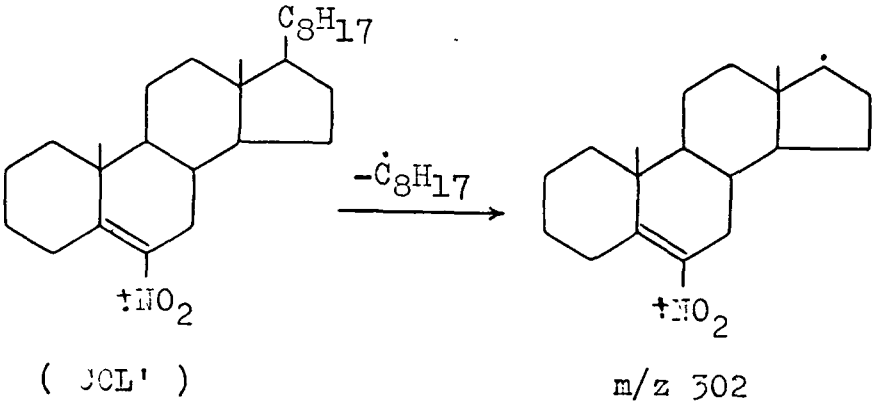
m/z 370

m/z 342



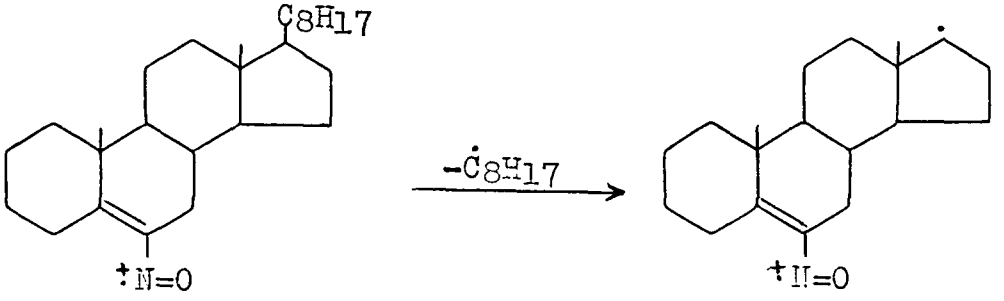
m/z 302, m/z 286 and m/z 272

These ions may be shown to arise by the loss of the side chain (C_8H_{17}) from the molecular ion, m/z 399 and m/z 385, respectively. The loss of the side chain on electron-impact is a common phenomenon in the mass spectrometry of steroidal compounds.



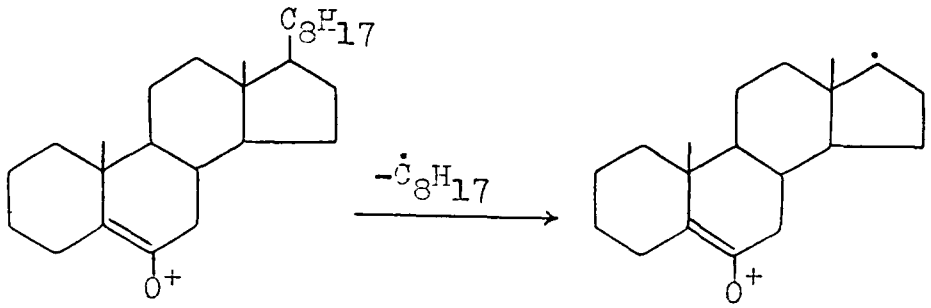
(JCL')

m/z 302



m/z 399

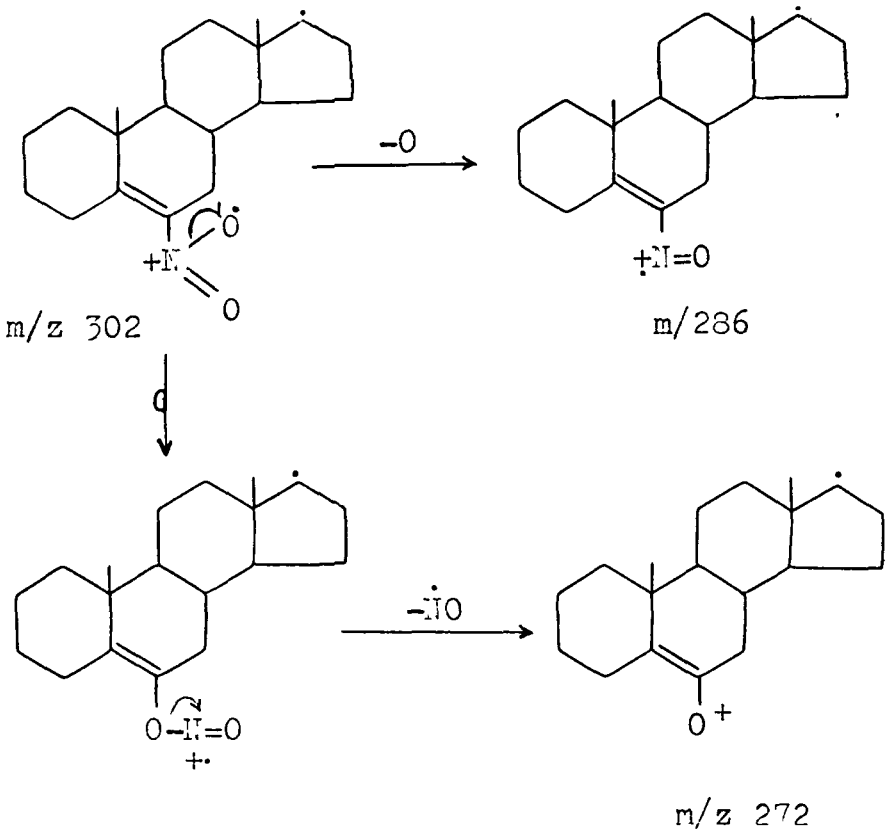
m/z 286



m/z 385

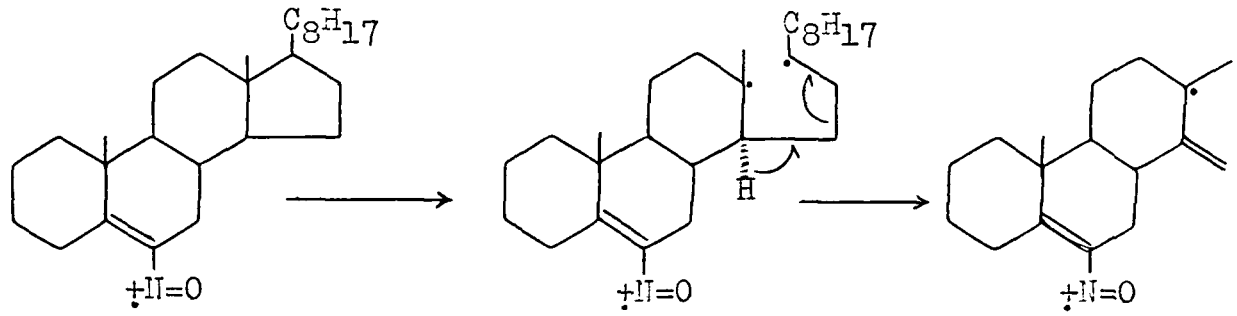
m/z 272

Alternatively, the ions m/z 286 and m/z 272 may also be shown to arise by the loss of oxygen and nitric oxide respectively from the ion m/z 302.



m/z 258

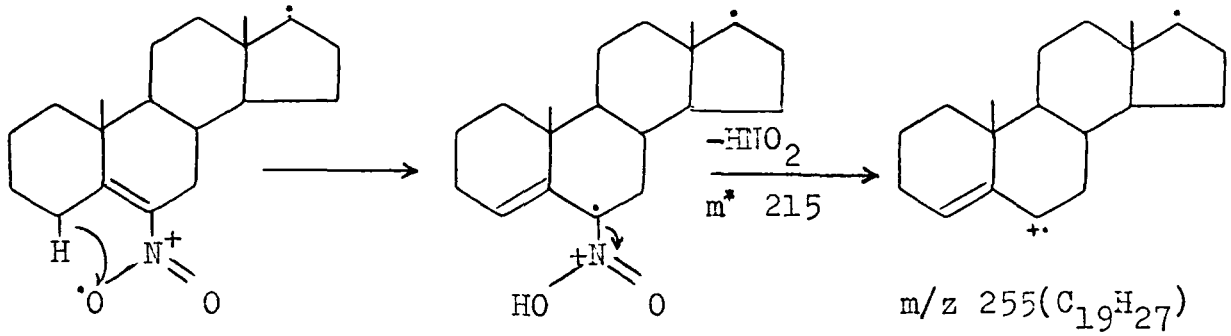
This ion may be shown to arise from the ion m/z 399 by the loss of the side chain along with part of the ring D.



m/z 399 m/z 258

m/z 255

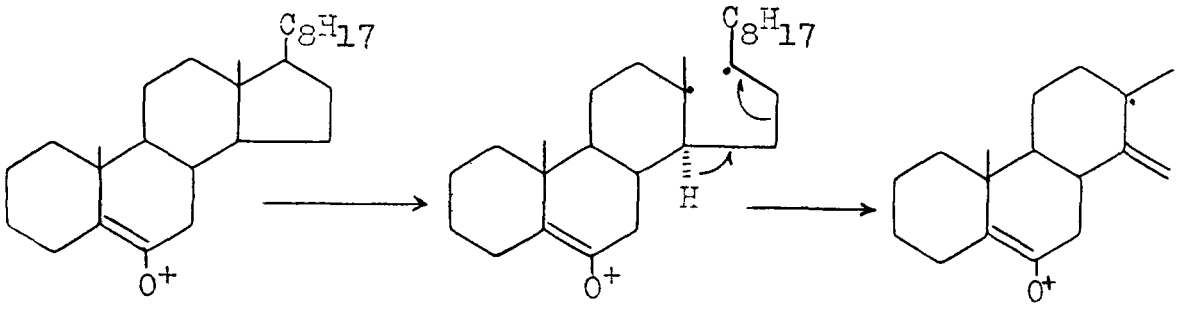
This ion most probably arises by the loss of the elements of nitrous acid from the ion m/z 302.



m/z 302 m/z 255($C_{19}H_{27}$)

m/z 244

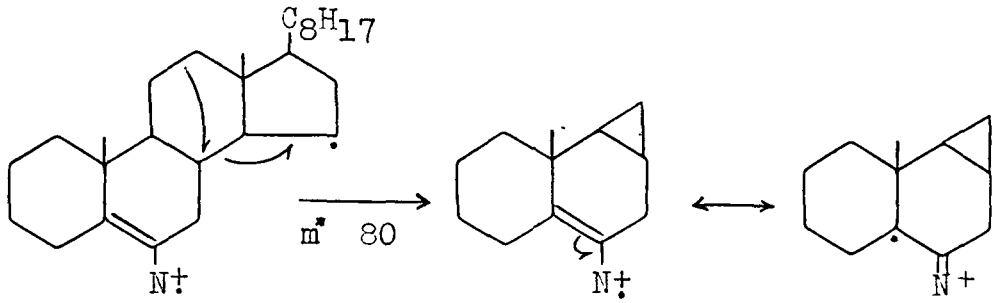
The ion m/z 244 may be formed by the loss of the side chain along with a part of the ring D from the ion m/z 385.



m/z 385 m/z 244

m/z 175 ($C_{12}H_{17}N$)

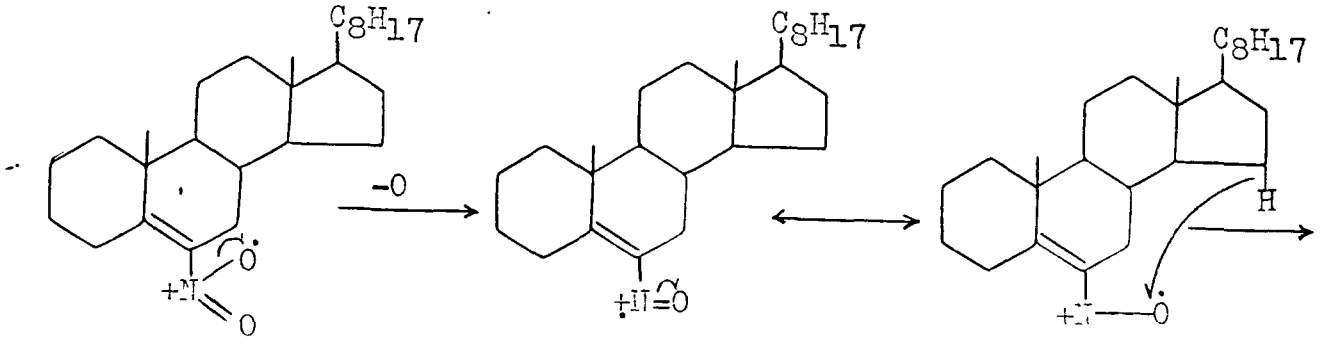
This ion is most probably obtained by the loss of side chain along with ring D and part of ring C from the ion m/z 382.



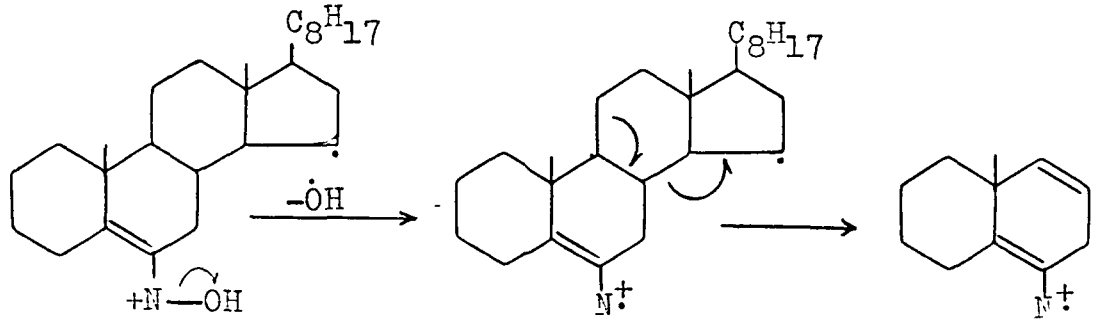
m/z 382 m/z 175 ($C_{12}H_{17}N$)

m/z 161 ($C_{11}H_{15}N$)

The ion m/z 161 can be shown to arise by the loss of rings C and D along with the side chain and the two oxygen atoms of the nitro group. The probable pathway involved in the formation of this ion can be shown as follows:



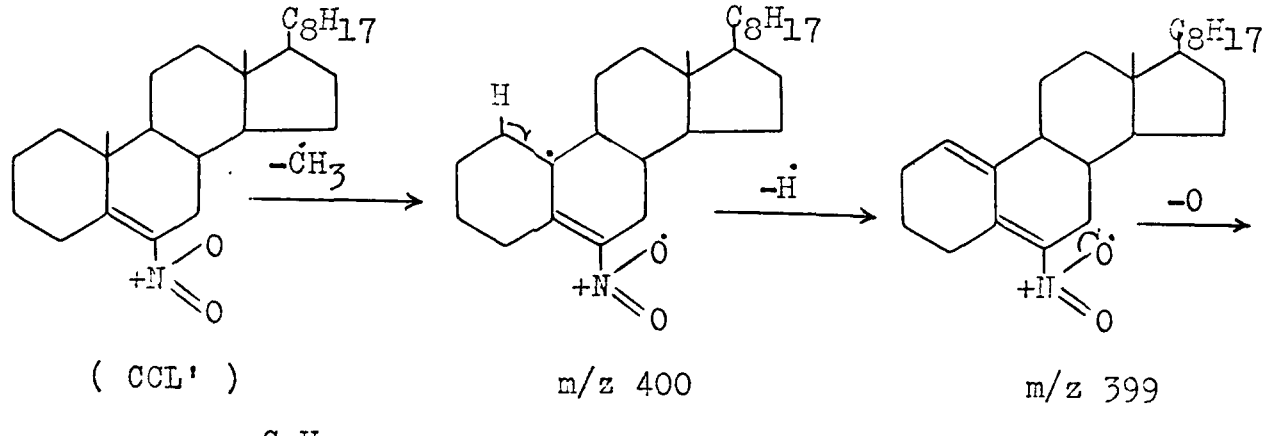
(CCL') m/z 399

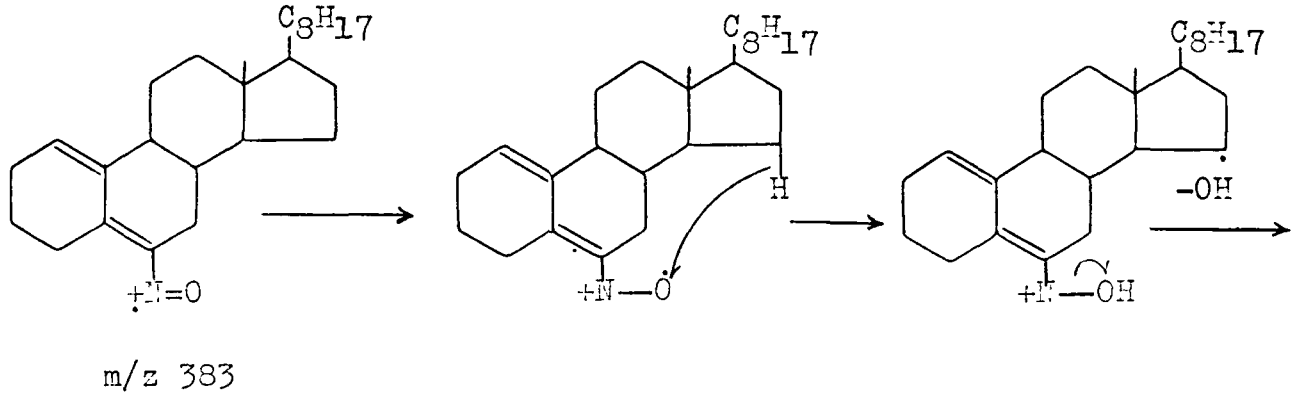


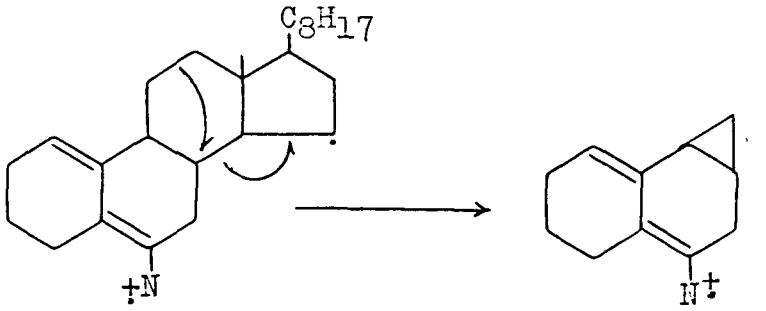
m/z 161($C_{11}H_{15}N$)

m/z 159 ($C_{11}H_{13}N$)

The ion m/z 159 ($C_{11}H_{13}N$) can be shown to arise by the following pathway.



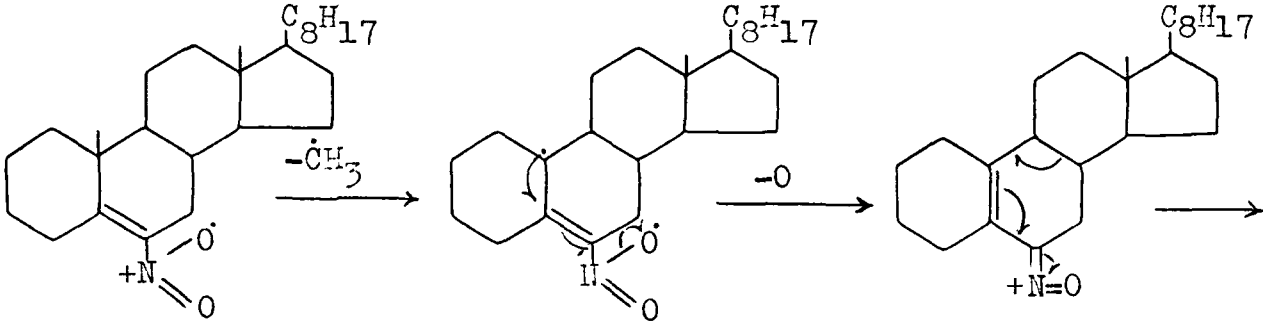




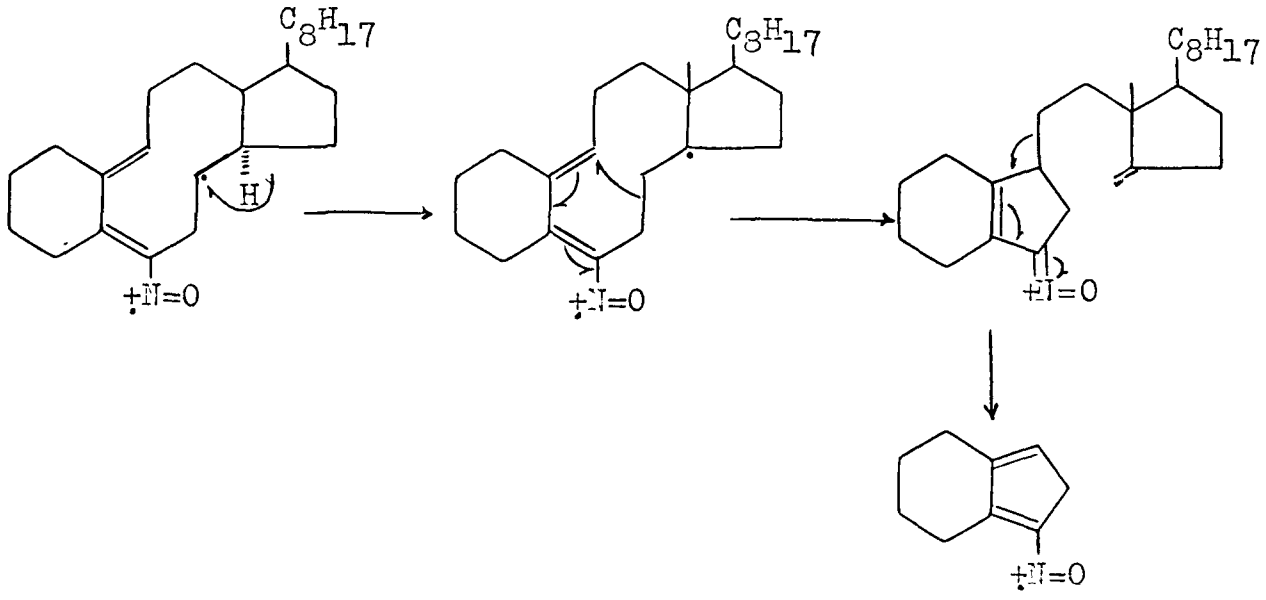
m/z 366 m/z 159($C_{11}H_{13}N$)

m/z 149 ($C_9H_{11}NO$)

The ion m/z 149 may be formed by the following sequence.



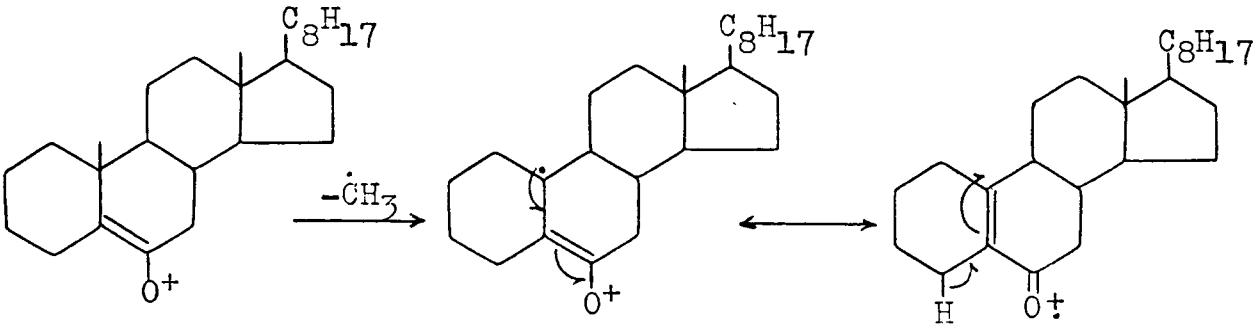
(CCL') m/z 400 m/z 384



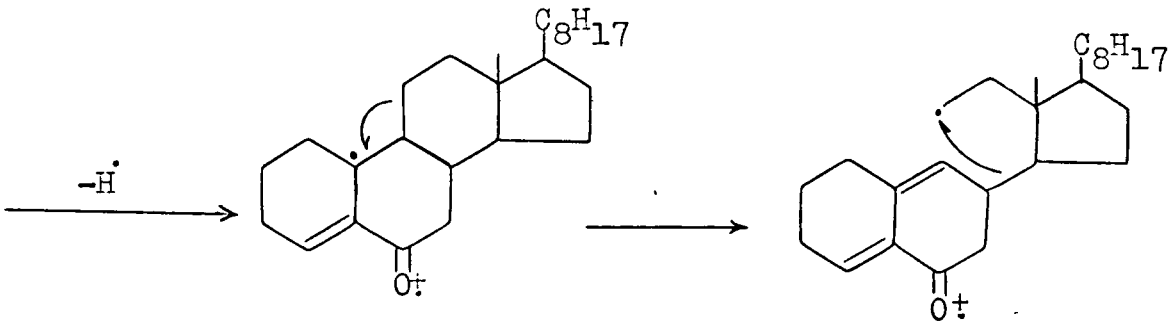
m/z 149($C_9H_{11}NO$)

m/z 147 ($C_{10}H_{11}O$)

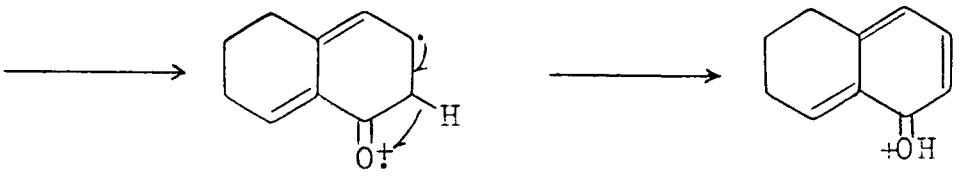
The ion m/z 147 may be shown to arise according to the following scheme.



m/z 385 m/z 370



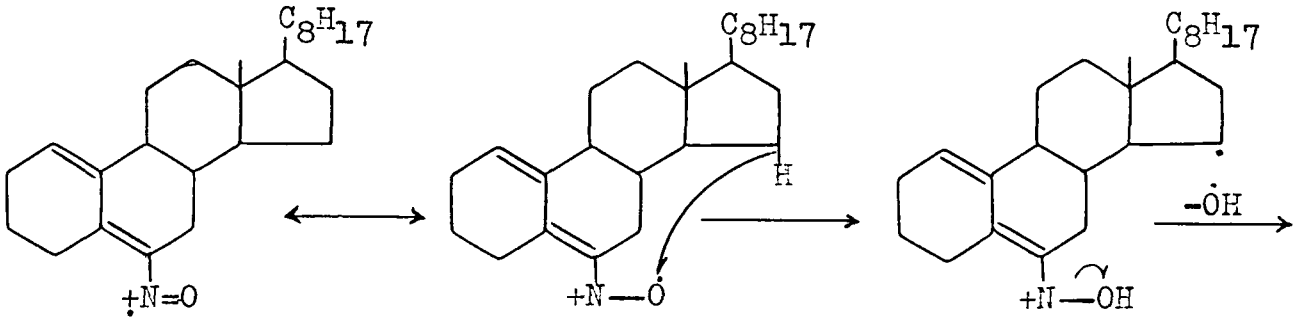
m/z 369



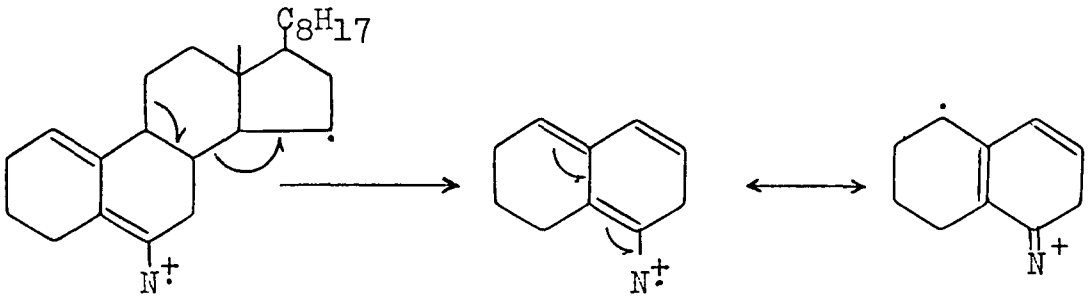
m/z 147($C_{10}H_{11}O$)

m/z 145 ($C_{10}H_{11}N$)

The ion m/z 145 ($C_{10}H_{11}N$) arises most probably by the fragmentation process shown below.



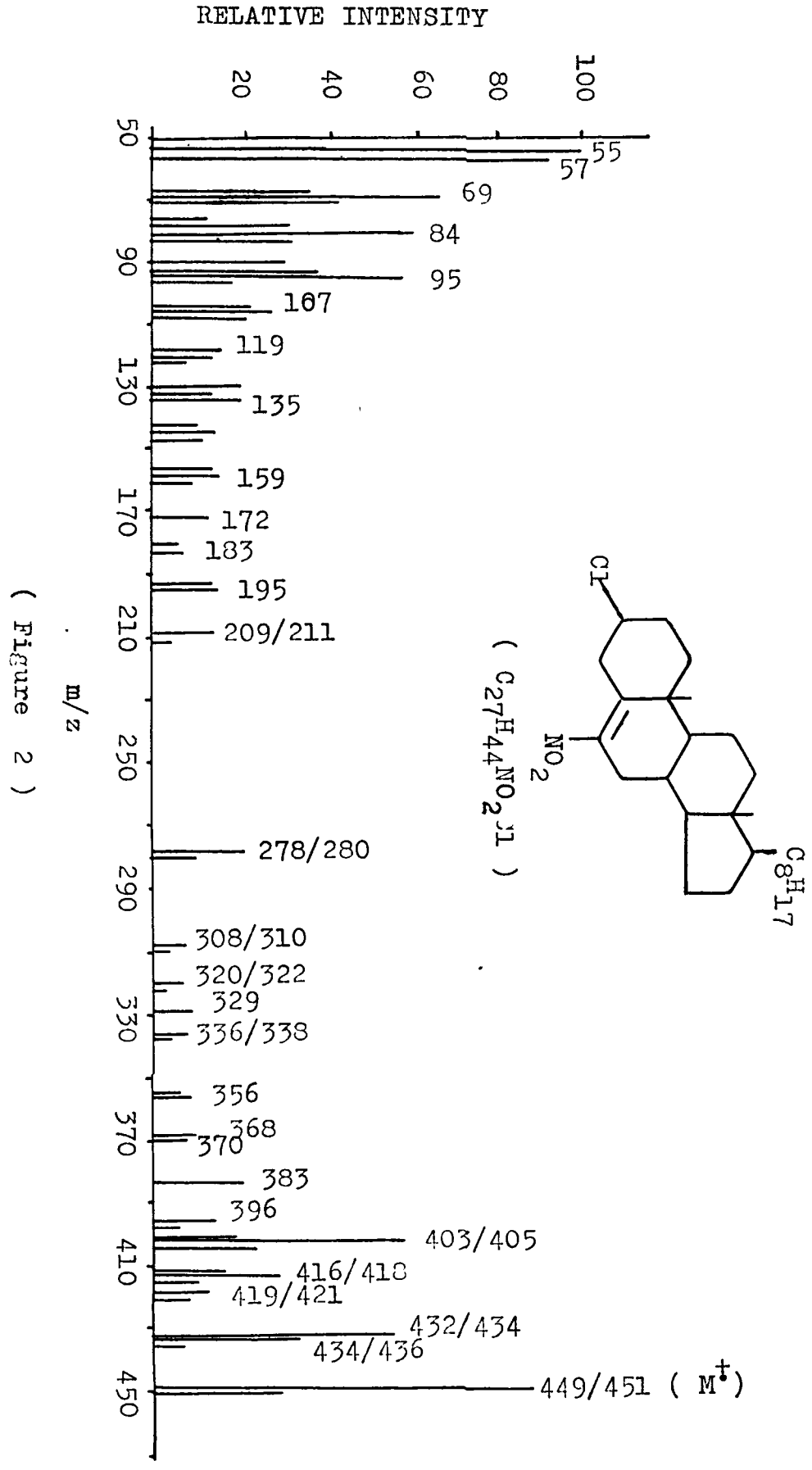
m/z 399



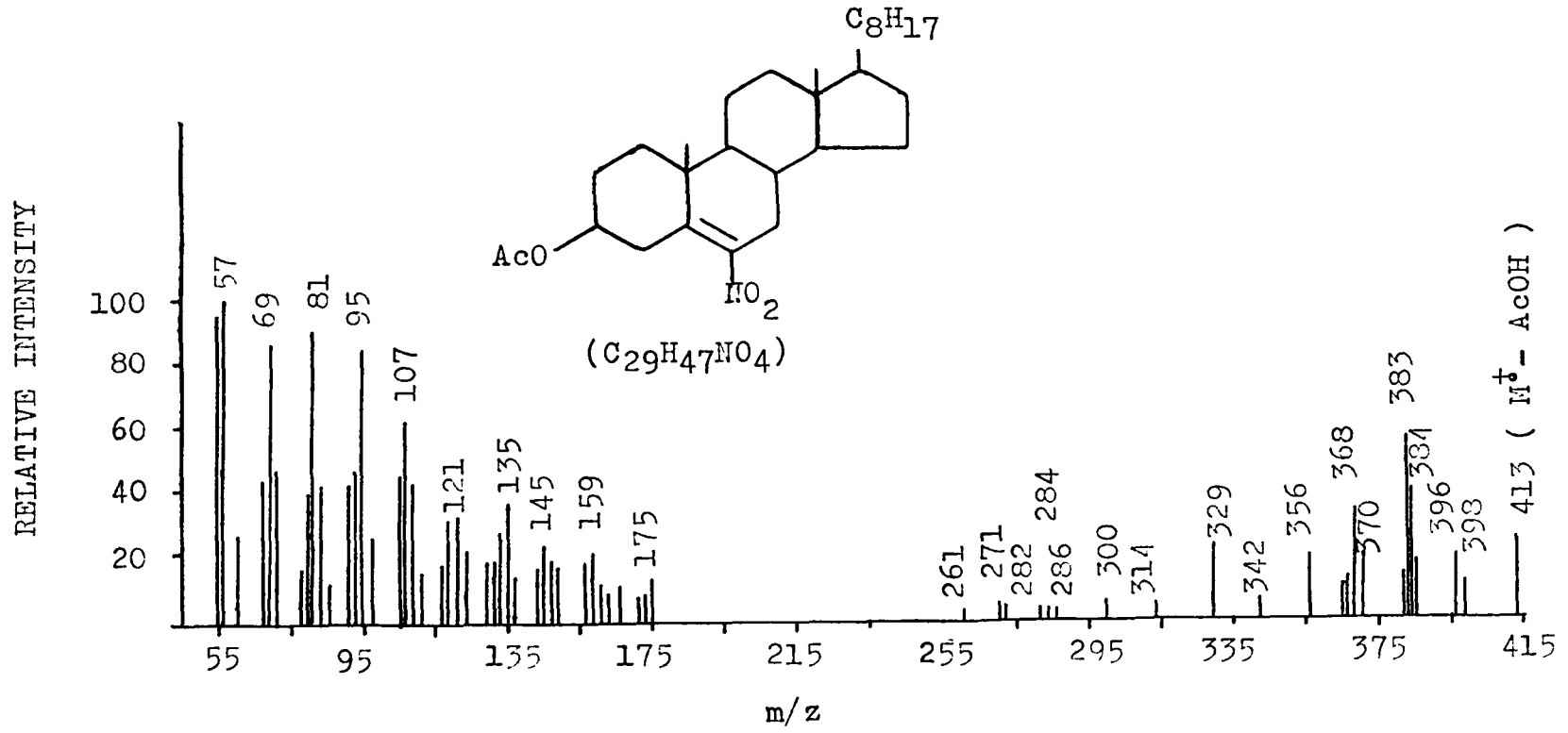
m/z 145 ($C_{10}H_{11}N$)

The mass spectra of 6-nitrocholest-5-en-3β-yl chloride (CCLV) and 6-nitrocholest-5-en-3β-yl acetate (CXLVIII) were comparable with that of the 6-nitrocholest-5-ene (CCL).

The mass spectrum of (CCLV) (Figure 2) gave the molecular ion peak at m/z 449/451. Most of the fragment ions were formed


RELATIVE INTENSITY
20
40
60
80
100
50
90
130
170
210
250
290
330
370
410
450
m/z
55
57
69
84
95
107
119
135
159
172
183
195
209/211
278/280
308/310
320/322
329
336/338
356
368
370
383
396
403/405
416/418
419/421
432/434
434/436
449/451 (M+)
(C27H44NO2Cl)
Cl
NO2
C8H17

(Figure 2)


RELATIVE INTENSITY
100
80
60
40
20
57
69
81
95
107
121
135
145
159
175
261
271
282
284
286
300
314
329
342
356
368
370
383
384
396
398
413 (M+ - AcOH)
55
95
135
175
215
255
295
335
375
415
m/z
C8H17
AcO
NO2
(C29H47NO4)

(Figure 3)

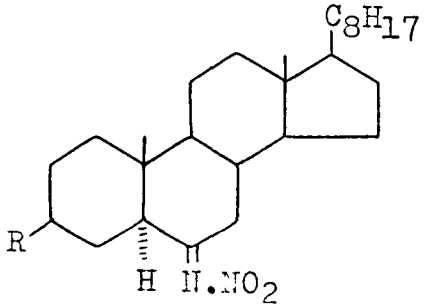
after the loss of HCl from the molecular ion[154]. The ions m/z 398, 396, 384, 383, 382, 381, 370, 368, 356, 355, 353, 330, 328, 318, 195, 193, 183, 172, 159, 157, 147, 145 and 143 obtained from (CCLV) are comparable with those obtained from (CCL). Some chlorine containing ions were also recorded in the spectrum of (CCLV) which were of special significance as they served as a label due to the isotopic nature of chlorine and helped to a great extent in the interpretation of the mass spectra of nitroolefins. Some of these ions were observed at m/z 434/436 (M^+-CH_3), 432/434 (M^+-OH), 419/421 (M^+-NO), 416/418 (M^+-O+OH), 403/405 (M^+-NO_2), 336/338 ($M^+-C_8H_{17}$), 320/322 (336/338-O), 308/310, 278/280 and 209/211. All these chlorine containing ions were in full correspondence with the ions obtained from (CCL).

The mass spectrum of 6-nitrocholest-5-en-3β-yl acetate (CXLVIII) (Figure 3) was quite similar to that of the simple nitroolefin (CCL). The highest mass peak in this spectrum was observed at m/z 413 which was most probably due to the initial loss of a molecule of acetic acid from the molecular ion (m/z 473) by a 1,2-elimination process[155]. Most of the fragment ions observed in the spectrum of (CXLVIII) corresponded to the ions obtained and discussed in the spectrum of (CCL) with a difference of two mass units. Some of these ions were m/z 398 (413-CH_3), 396 (413-OH), 383 (413-NO), 382 (398-O), 370 (396-CH≡CH), 368 (398-NO), 367 (413-NO_2), 366 (413-HNO_2), 356 (383-CH≡CH), 355 (356-H), 342 (368-CH≡CH), 300 (413-C_8H_{17}), 284 (300-O), 173 ($C_{12}H_{15}N$), 159 ($C_{11}H_{13}N$), 157 ($C_{11}H_{11}N$), 147 (C_9H_9NO), 145 ($C_{10}H_9O$) and 143 ($C_{10}H_9N$).

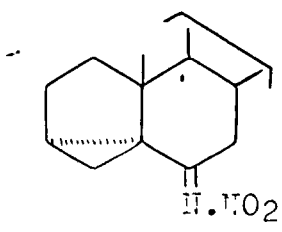
B. N-NITROSTEROIDS

A survey of the literature revealed that though a number of C-nitro compounds have been subjected to the mass spectral studies but no significant mass spectrometric work has been carried out on N-nitro compounds. In our present work we have undertaken the mass spectral studies on some of the steroidal N-nitro compounds called nitrimines. We have made an attempt to see how the nitro group bonded to an imine function influences the fragmentation pathway. These studies have assisted in assigning the correct structures to these compounds.

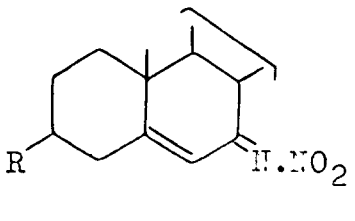
The nitrimines selected for the present studies are 6-nitrimino-5α-cholestane (CLXIII), 6-nitrimino-5α-cholestan-3β-yl acetate (LIV), 6-nitrimino-3α,5α-cyclo-5α-cholestane (CLXXIII), 7-nitriminocholest-5-ene (CLXXXIII), 7-nitrimino-cholest-5-en-3β-yl acetate (LV) and anti- and syn- forms of 3-nitriminocholest-4-ene (CLXXVI) and (CLXXVII), respectively.



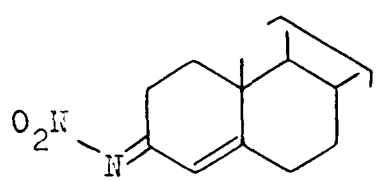
(CLXIII) R = H
(LIV) R = OAc



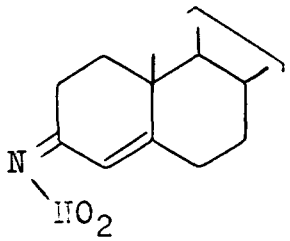
(CLXXIII)



(CLXXXIII) R = H
(LV) R = OAc



(CLXXVI)



(CLXXVI)

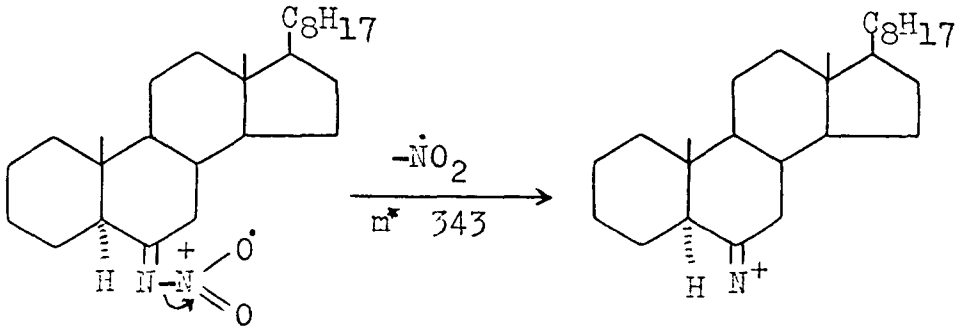
The mass spectra of all the nitrimines were conspicuous by the presence of a very insignificant molecular ion peak. In some cases the molecular ion peak did not appear at all and the highest mass peak was obtained either after the loss of NO or NO_2 from the molecular ion. The base peak in almost all the spectra was observed due to the loss of an NO_2 radical from the molecular ion. The loss of NO was indicative of the fact that like the nitroolefins, the nitro group in nitrimines also undergoes rearrangement under the electron-impact to the isomeric nitrite form prior to the fragmentation. In our present discussion, only the mass spectra of 6-nitrimino-5α-cholestane (CLXIII) and 7-nitriminocholest-5-ene (CLXXXIII) have been discussed in some detail as they may be considered as the model for steroidal 6-,and 7-nitrimines. A comparison has been made with other nitrimines. The mass spectra of the anti- and syn- forms of 3-nitriminocholest-4-ene (CLXXVI) and (CLXXVII), respectively have also been discussed in an attempt to rationalize the differences, if any, between these isomeric nitrimines. The fragmentation pathways suggested are supported in some cases by appropriate metastable peaks. The mechanistic schemes proposed

are tentative in the absence of mass spectra of appropriate deuterated analogues and accurate mass measurements of the fragment ions.

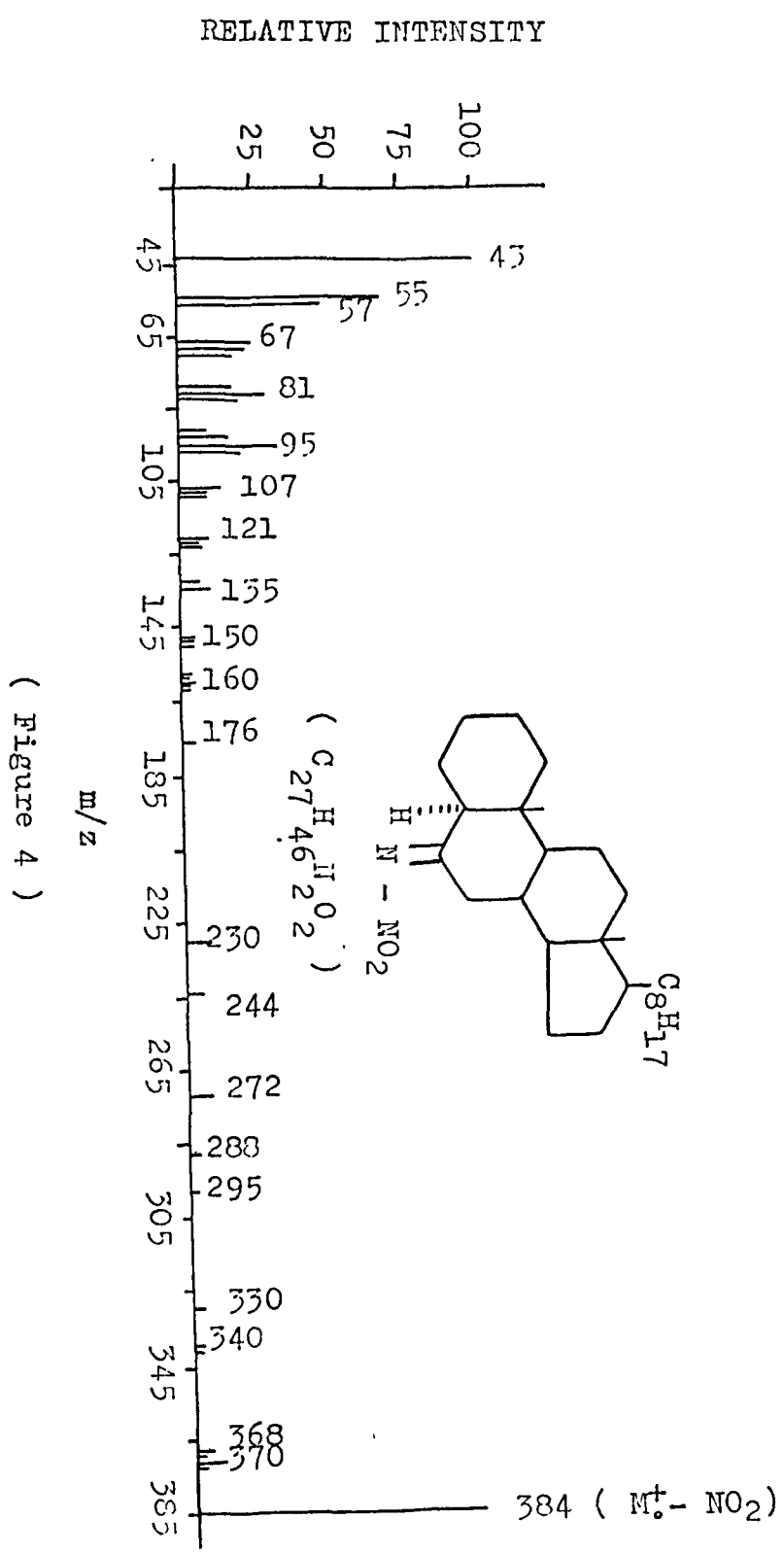
The mass spectrum of 6-nitrimino-5α-cholestane (CLXIII) (Figure 4) was conspicuous by the absence of the molecular ion peak. The highest mass peak was observed at m/z 384, most probably after the initial loss of NO_2 from the molecular ion (m/z 430). The other fragment ions were observed at m/z 370, 369, 341, 340, 330, 298, 288, 272, 244, 230, 176, 163, 162, 161, 160, 149, 148, 147 and lower mass peaks. The genesis of some of the salient ions has been shown in the following schemes:

m/z 384

The ion m/z 384 was the highest mass peak observed in the spectrum of (CLXIII) and constituted the base peak of the spectrum. This ion may be formed by the initial loss of NO_2 from the molecular ion, i.e. m/z 430 ($C_{27}H_{46}N_2O_2$).



(CLXII') m/z 384


RELATIVE INTENSITY
25
50
75
100
45
43
55
57
65
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81
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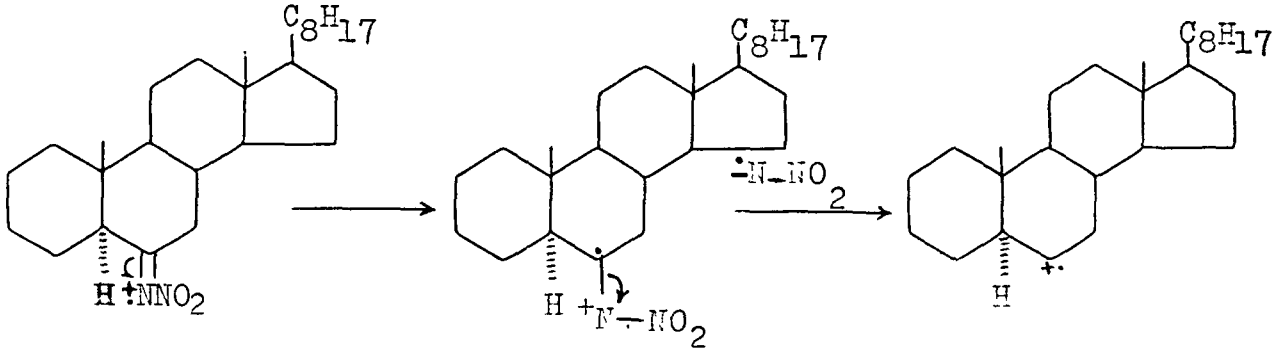
105
107
121
135
145
150
160
176
185
225
230
244
265
272
288
295
305
330
340
345
368
370
385
384 (M+. - NO2)
m/z
(C27H46N2O2)
H
N - NO2
C8H17

(Figure 4)

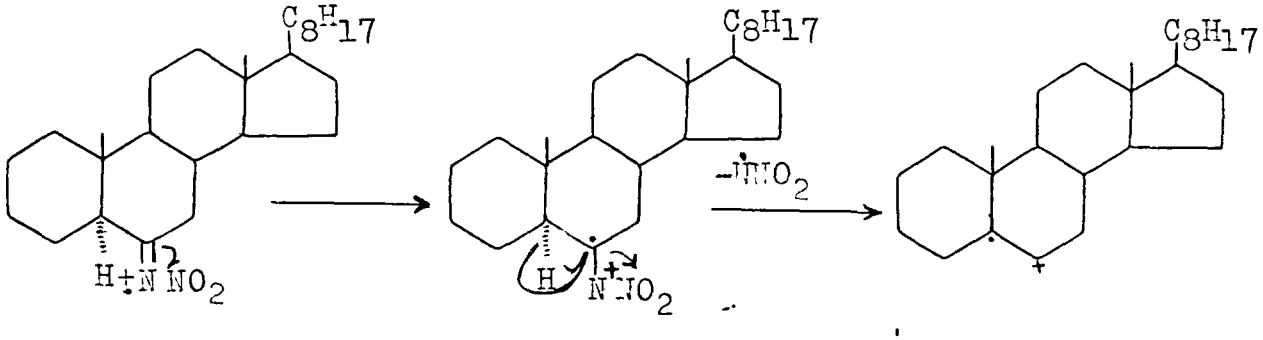
m/z 370

The ion m/z 370 may be shown to arise from the molecular ion by the loss of $N.NO_2$ to give a species equivalent to the corresponding olefin.



(CLXIII') m/z 370 ($C_{27}H_{46}$)

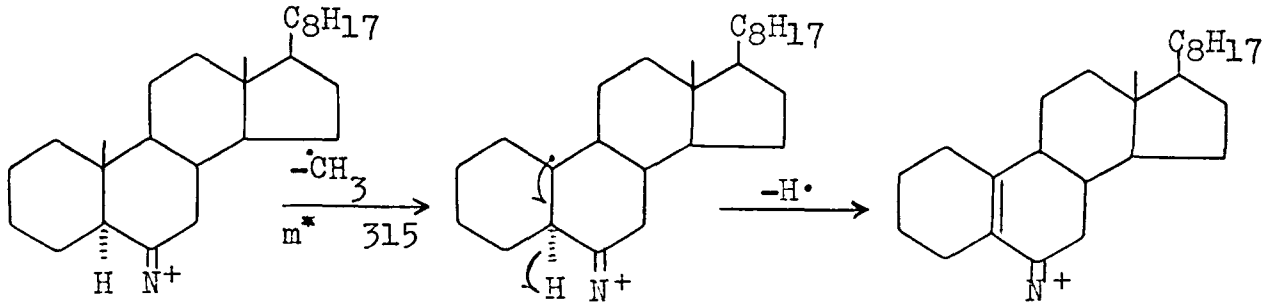
OR



(CLXIII') m/z 370 ($C_{27}H_{46}$)

m/z 369 and m/z 368

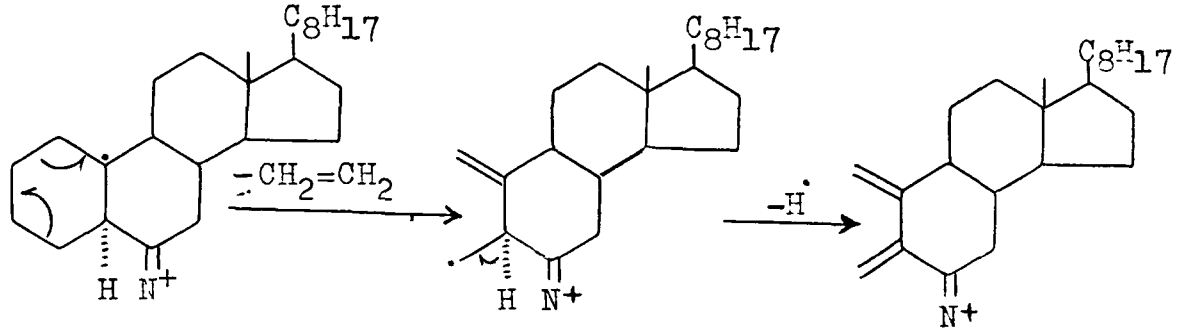
The ion m/z 369 most probably, arises by the loss of a methyl radical from the ion m/z 384, which subsequently loses a hydrogen radical to give the ion m/z 368.



m/z 384 m/z 369 m/z 368

m/z 341 and m/z 340

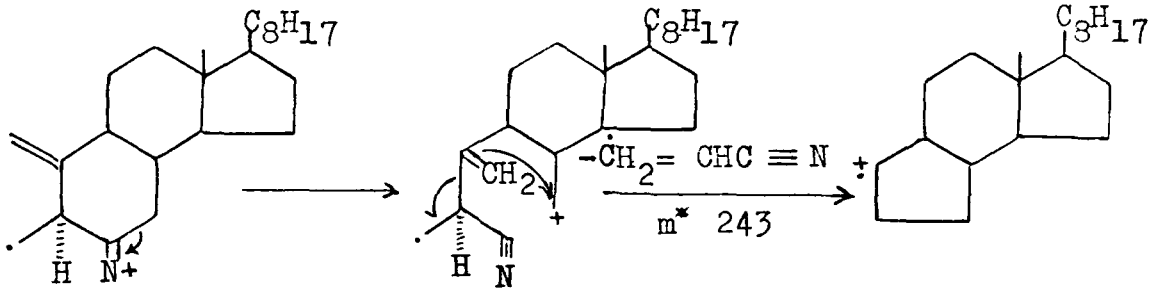
The ion m/z 341 may arise from the ion m/z 369 by the loss of ethylene from ring A. Further loss of a hydrogen radical from the ion m/z 341 gives the ion m/z 340.



m/z 369 m/z 341 m/z 340

m/z 288

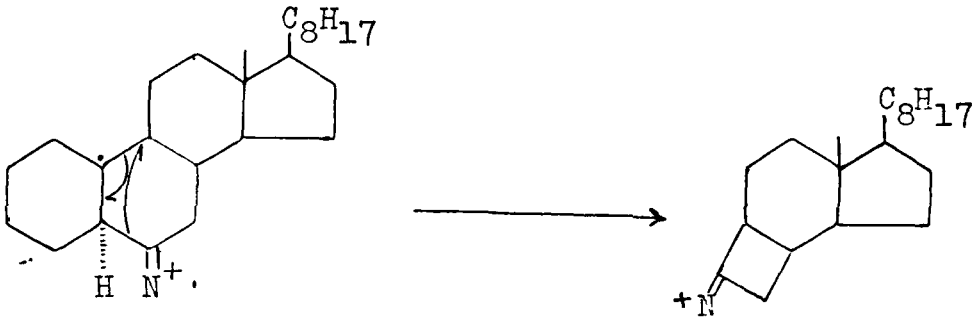
This ion most probably arises by the loss of a nitrile species from the ion m/z 341.



m/z 341

m/z 288

Alternatively, the ion m/z 288 may also arise by the loss of ring A from the ion m/z 369 as shown below.

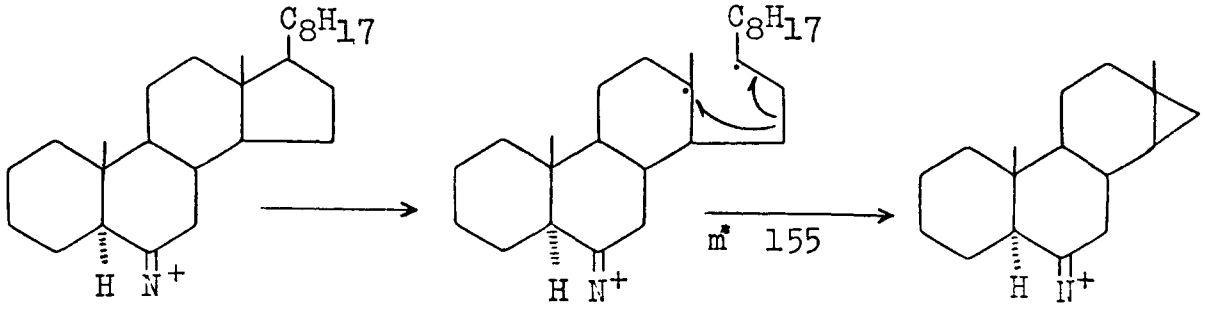


m/z 369

m/z 288

m/z 244

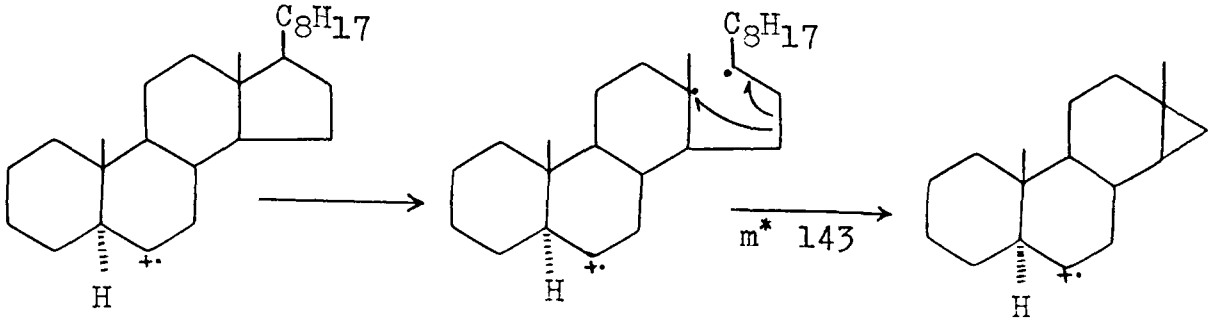
The ion m/z 244 may be shown to arise by the loss of side chain along with a part of the ring D from the ion m/z 384. Such a loss of the side chain and part of ring D is a common phenomenon in the mass spectra of steroidal compounds.



m/z 384 m/z 244

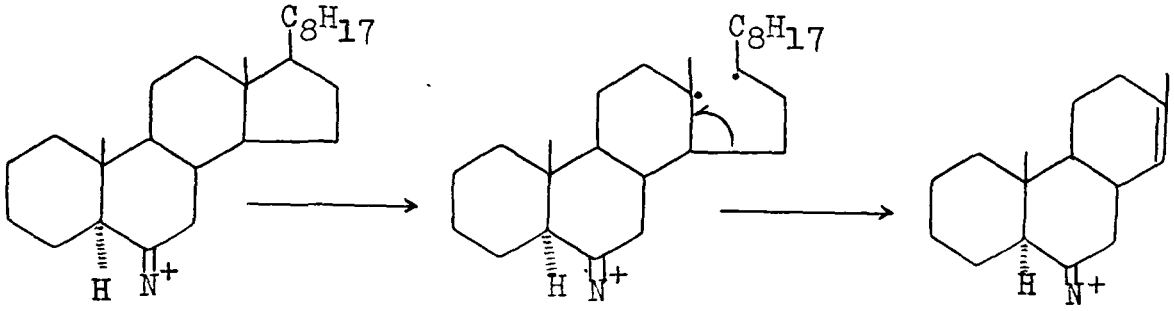
m/z 230

This ion is probably formed by the loss of side chain and part of the ring D from the ion m/z 370.



m/z 370 m/z 230

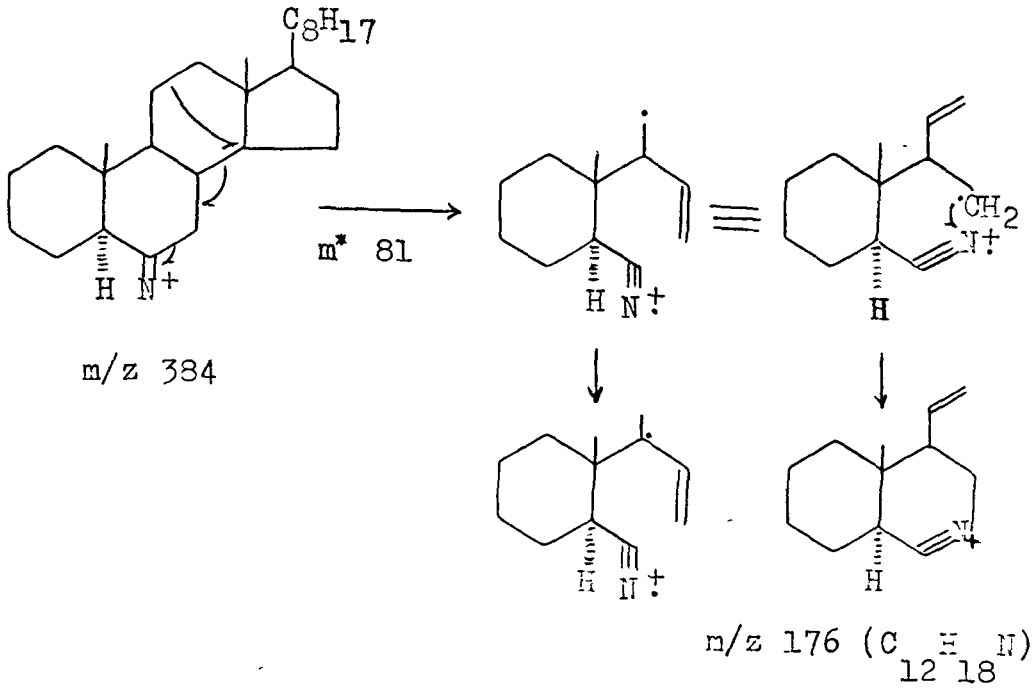
Alternatively, the ion m/z 230 can also arise by the loss of side chain along with ring D from the ion m/z 384.



m/z 384 m/z 230

m/z 176 ($C_{12}H_{18}N$)

This ion may be shown to arise by the loss of rings C and D along with the side chain as shown below.

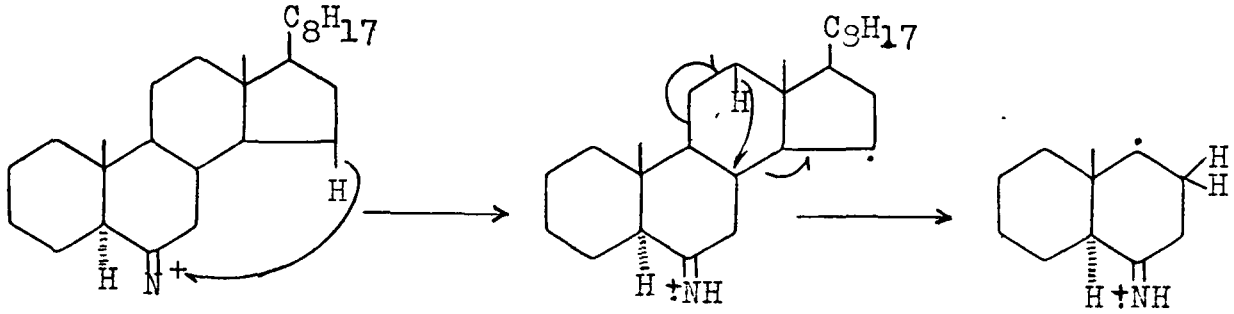


m/z 384

m/z 176 ($C_{12}H_{18}N$)

m/z 164 ($C_{11}H_{18}N$)

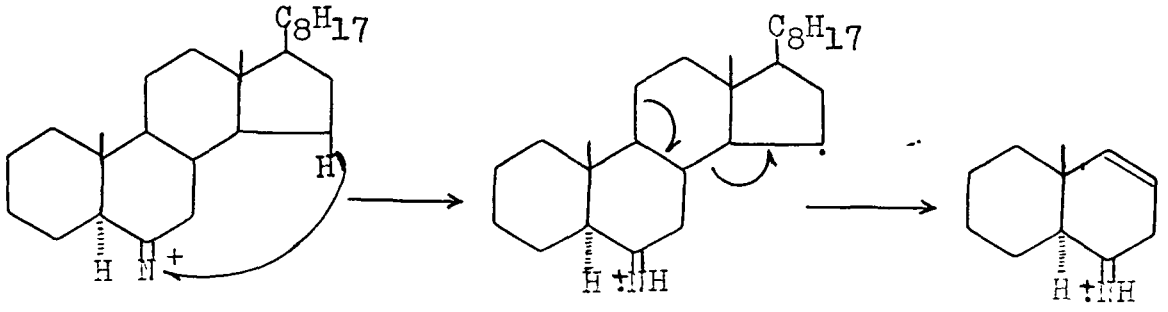
The ion m/z 164 can be shown to arise by the following sequence.



m/z 384 m/z 164 ($C_{11}H_{18}N$)

m/z 163 ($C_{11}H_{17}N$)

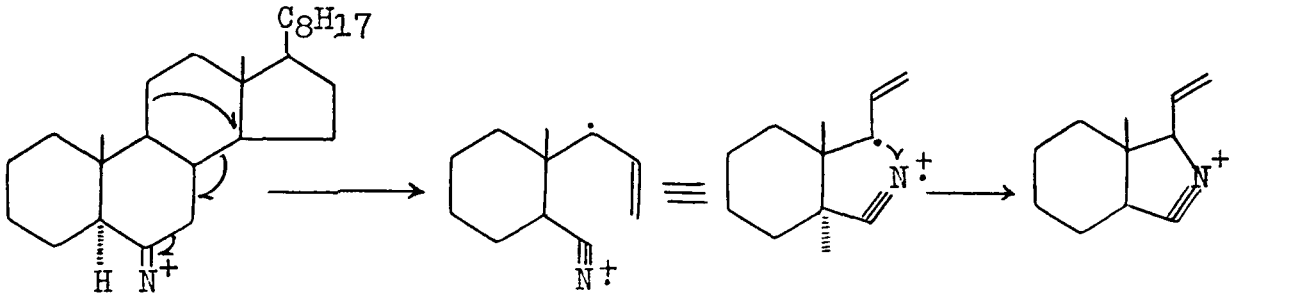
The ion m/z 163 ($C_{11}H_{17}N$) arises from the ion m/z 384 by the loss of rings B and C along with the side chain as shown in the following scheme.



m/z 384 m/z 163 ($C_{11}H_{17}N$)

m/z 162 ($C_{11}H_{16}N$)

This ion most probably, arises as a nitrile species formed from ringsA and B.

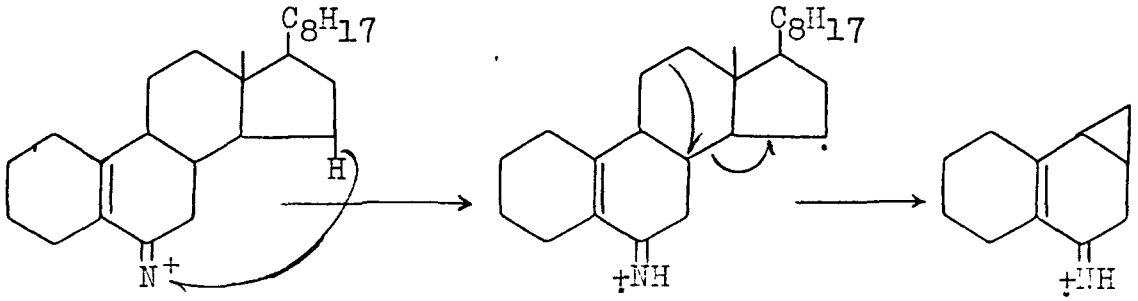


m/z 384

m/z 162($C_{11}H_{16}N$)

m/z 161 ($C_{11}H_{15}N$)

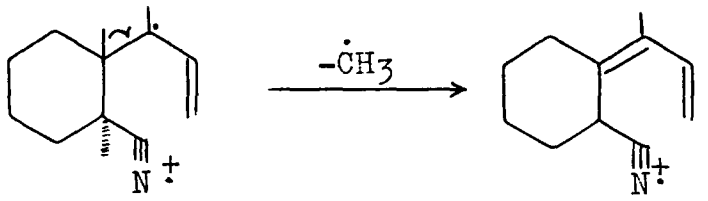
The ion m/z 161 arises most probably from the ion m/z 368 by the loss of the side chain along with ring D and part of ring C. It may also be shown to arise by the loss of a methyl radical from the ion m/z 176.



m/z 368

m/z 161 ($C_{11}H_{15}N$)

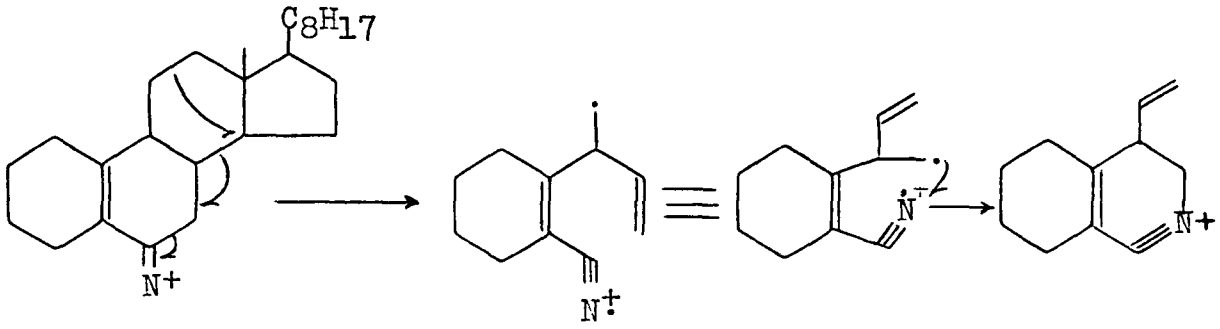
OR



m/z 176($C_{12}H_{18}N$) m/z 161 ($C_{11}H_{15}N$)

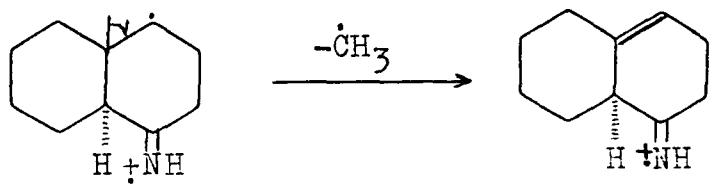
m/z 160 ($C_{11}H_{14}N$)

The ion m/z 160 may be shown to arise by the following sequence from the ion m/z 368.



m/z 368 m/z 160 ($C_{11}H_{14}N$)

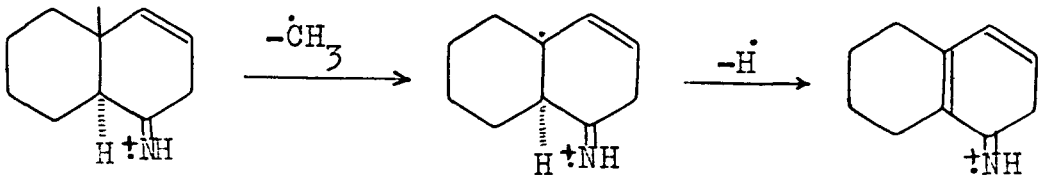
m/z 149 ($C_{10}H_{15}N$)



m/z 164 ($C_{11}H_{18}N$) m/z 149 ($C_{10}H_{15}N$)

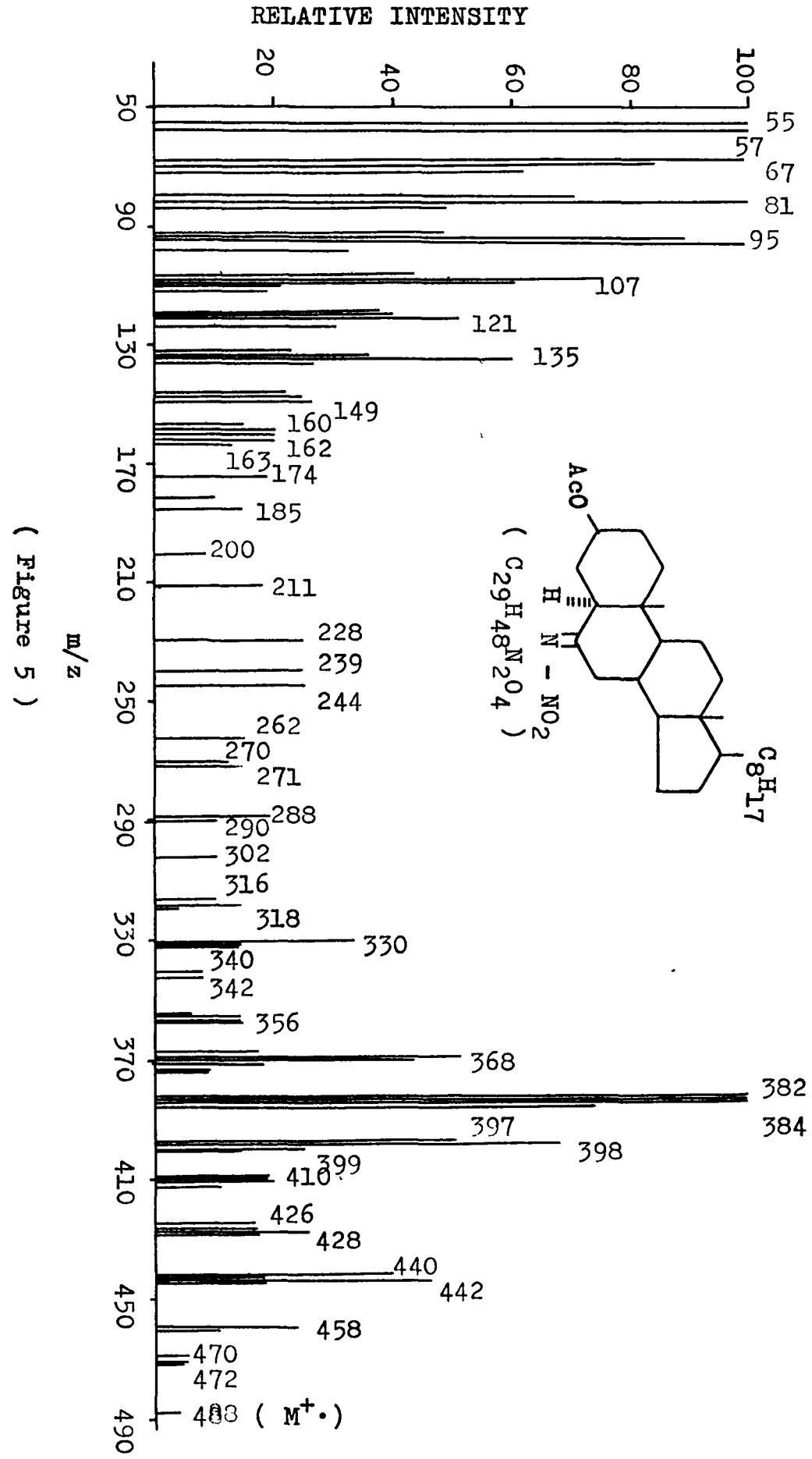
m/z 148 ($C_{10}H_{14}N$) and m/z 147 ($C_{10}H_{13}N$)

The ion m/z 148 arises by the loss of a methyl radical from the ion m/z 163. Further loss of hydrogen from the ion m/z 148 gives the ion m/z 147.



m/z 163 ($C_{11}H_{17}N$) m/z 148 ($C_{10}H_{14}N$) m/z 147 ($C_{10}H_{13}N$)

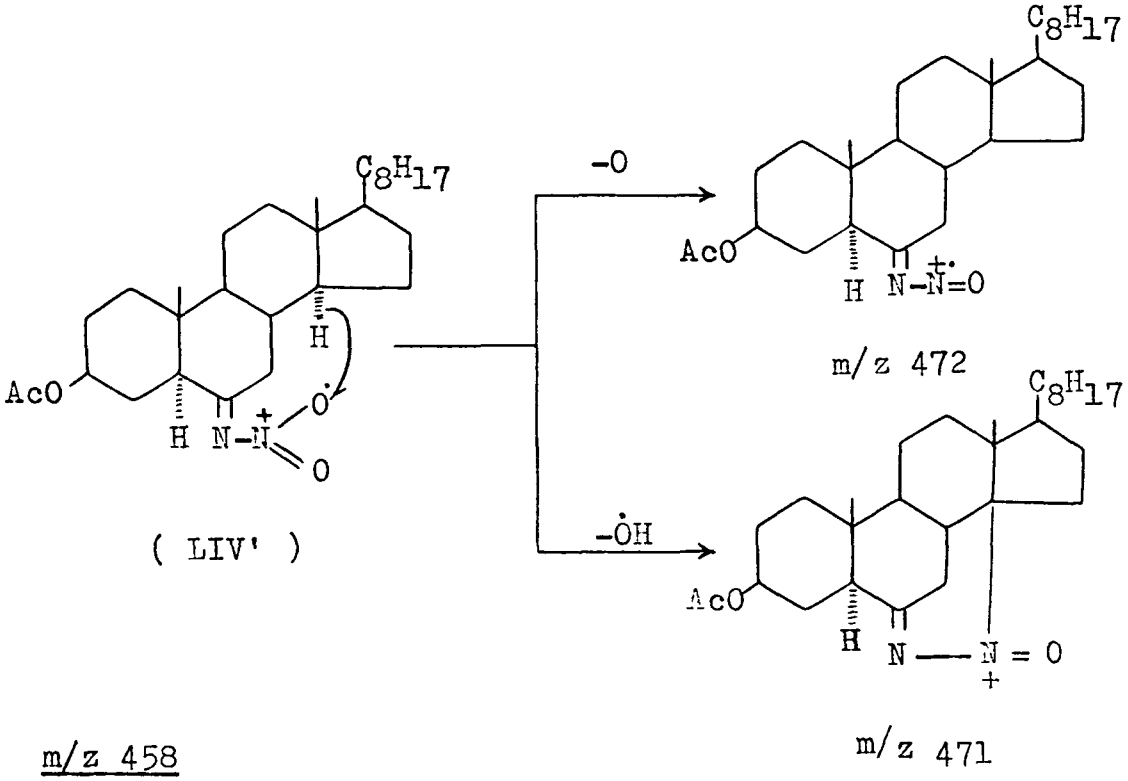
The mass spectrum of 6-nitrimino-5α-cholestan-3β-yl acetate (LIV) (Figure 5) was comparable with that of (CLXIII). It showed a very weak molecular ion peak at m/z 488. The loss of NO_2 along with AcOH from the molecular ion was responsible for the base peak at m/z 382. The mass spectrum of the acetoxynitrimine (LIV) also showed the fragment ions in between the molecular ion (m/z 488) and the base peak (m/z 382) which could not be recorded in the mass spectrum of the nitrimine (CLXIII). The genesis of some of these fragment ions has been shown in the following schemes.


RELATIVE INTENSITY
20
40
60
80
100
50
90
130
170
210
250
290
330
370
410
450
490
m/z
55
57
67
81
95
107
121
135
149
160
162
163
174
185
200
211
228
239
244
262
270
271
288
290
302
316
318
330
340
342
356
368
382
384
397
398
399
410
426
428
440
442
458
470
472
488 (M+·)
AcO
H
N
N - NO2
(C29H48N2O4)
C8H17

(Figure 5)

m/z 472 and m/z 471

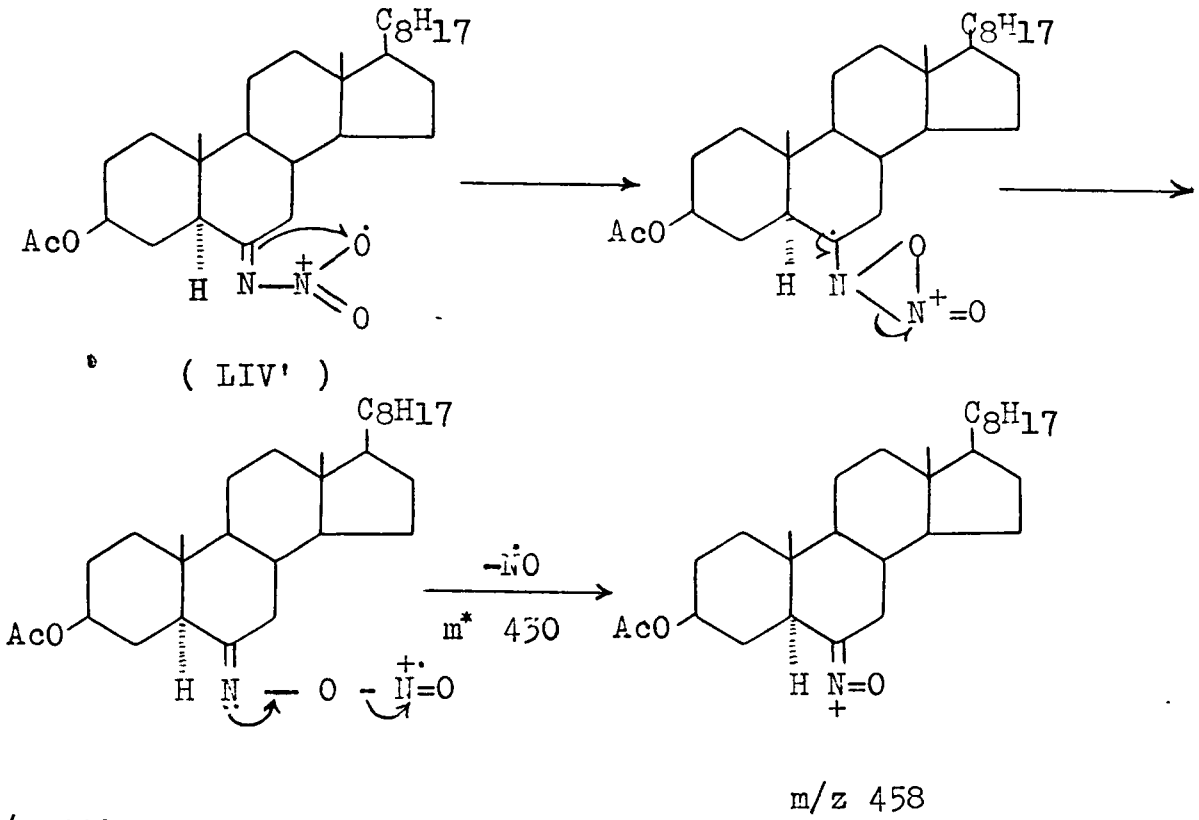
The ion m/z 472 arises most probably, by the loss of oxygen of the nitrogroup from the molecular ion. The ion m/z 471 may arise by the loss of a hydroxy radical from the molecular ion.



(LIV')

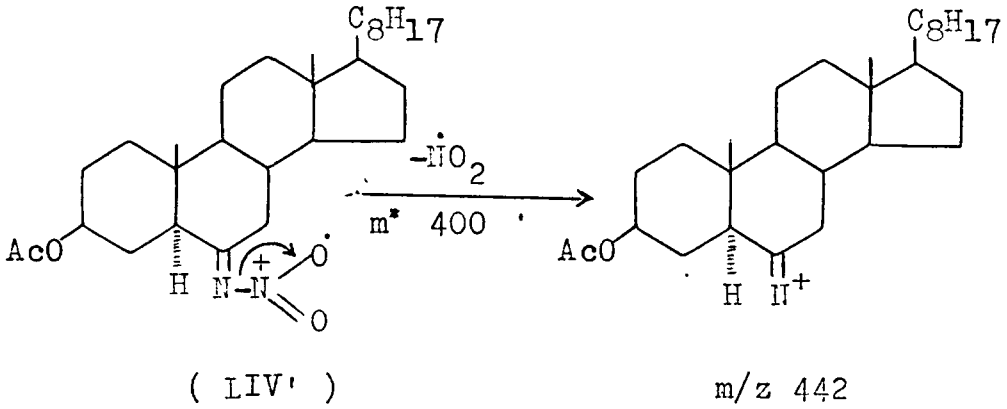
m/z 458

The ion m/z 458 arises most probably by the loss of nitric oxide (NO) from the molecular ion. Such a loss from the molecular ion can be explained on the basis of the rearrangement of the nitrimine to the isomeric oxime nitrite which may then lose NO to give the ion m/z 458. This process is similar to the one observed in nitroolefins where the nitro group under the electron-impact rearranges to nitrite form prior to fragmentation[97].



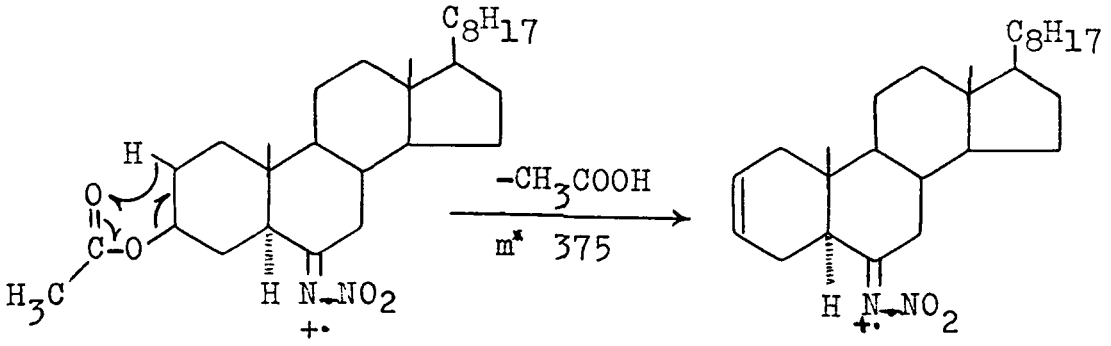
m/z 442

The ion m/z 442 may be shown to arise by the loss of NO_2 from the molecular ion.

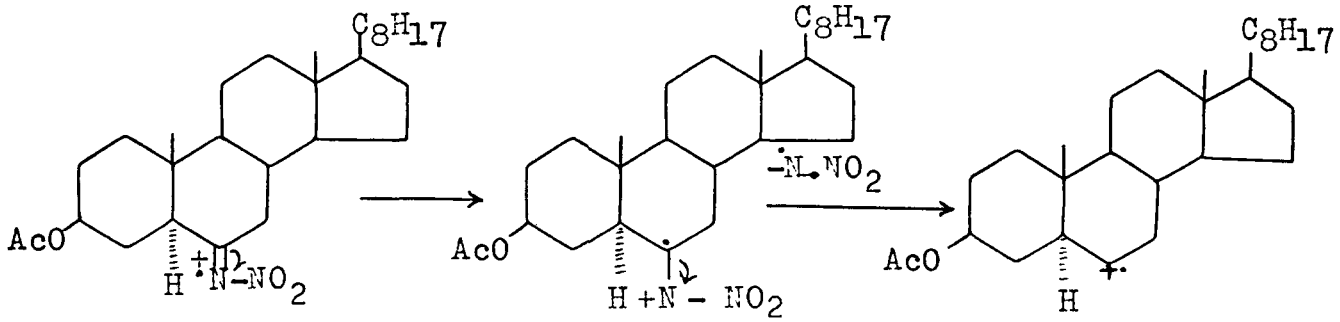


m/z 428

This ion may be accounted for by the loss of either a molecule of acetic acid by 1,2-elimination process[152] or $N.NO_2$ from the molecular ion.

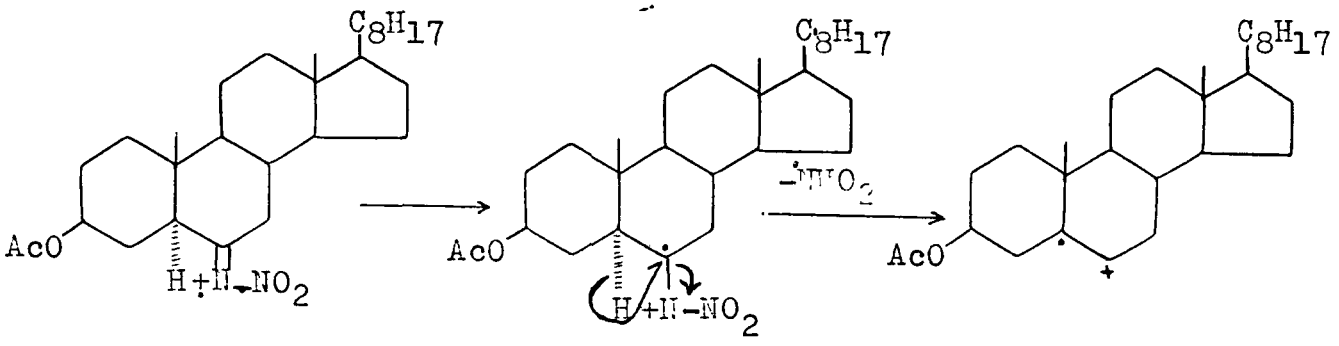


(LIV') m/z 428

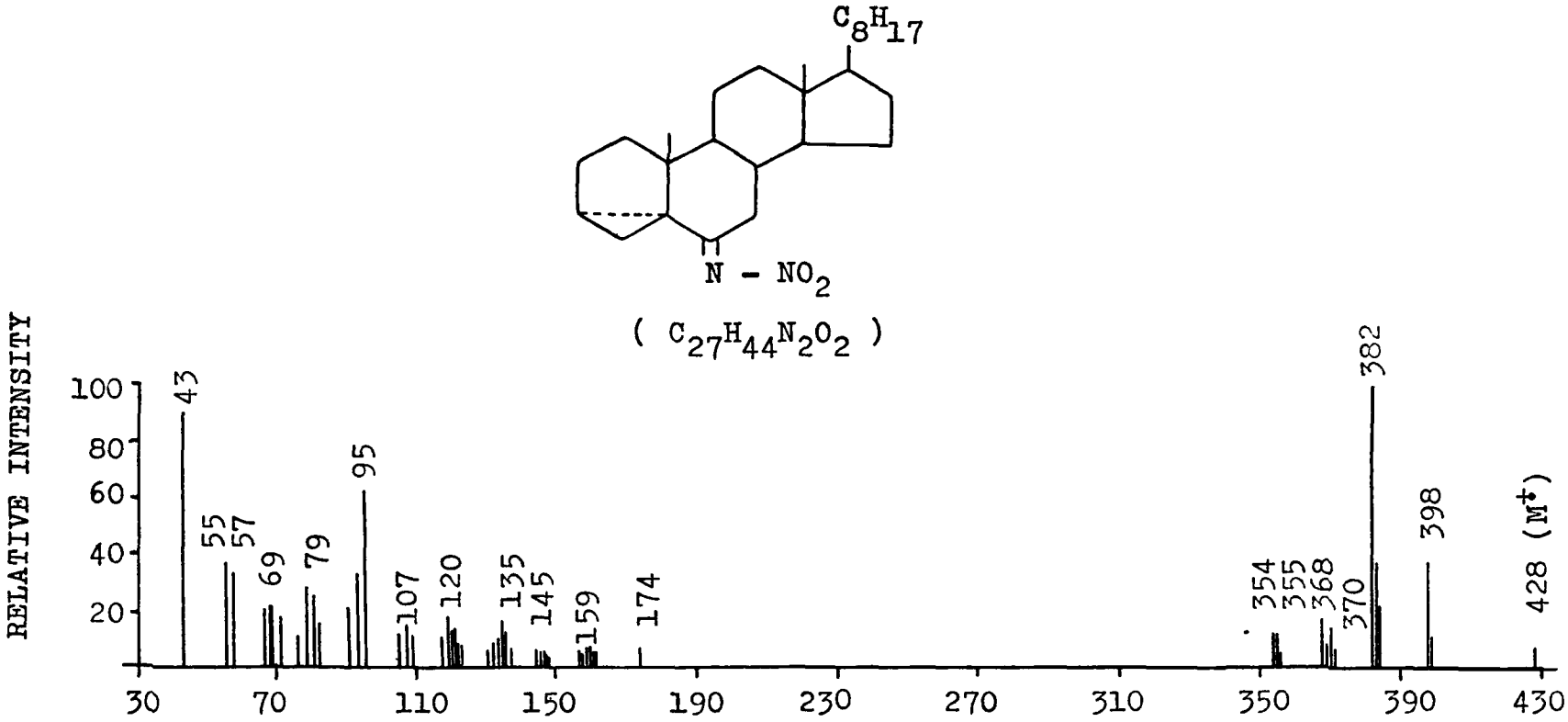


(LIV') m/z 428

OR



(LIV') m/z 428


C_8H_{17}
N - NO_2
($C_{27}H_{44}N_2O_2$)
RELATIVE INTENSITY
100
80
60
40
20
43
55
57
69
79
95
107
120
135
145
159
174
354
355
368
370
382
398
428 (M^+)
30
70
110
150
190
230
270
310
350
390
430
m/z

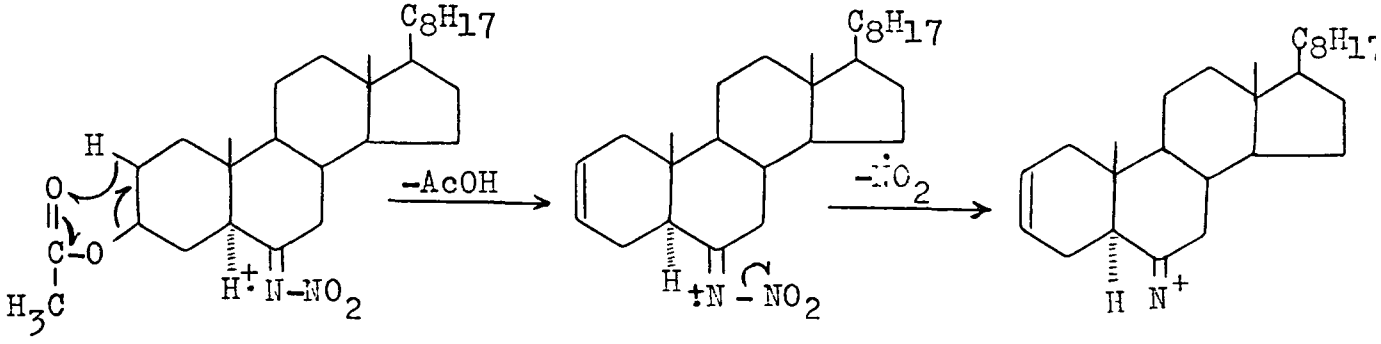
(Figure 6)

m/z 398

This ion arises by the loss of a molecule of acetic acid from the ion m/z 458.

m/z 382

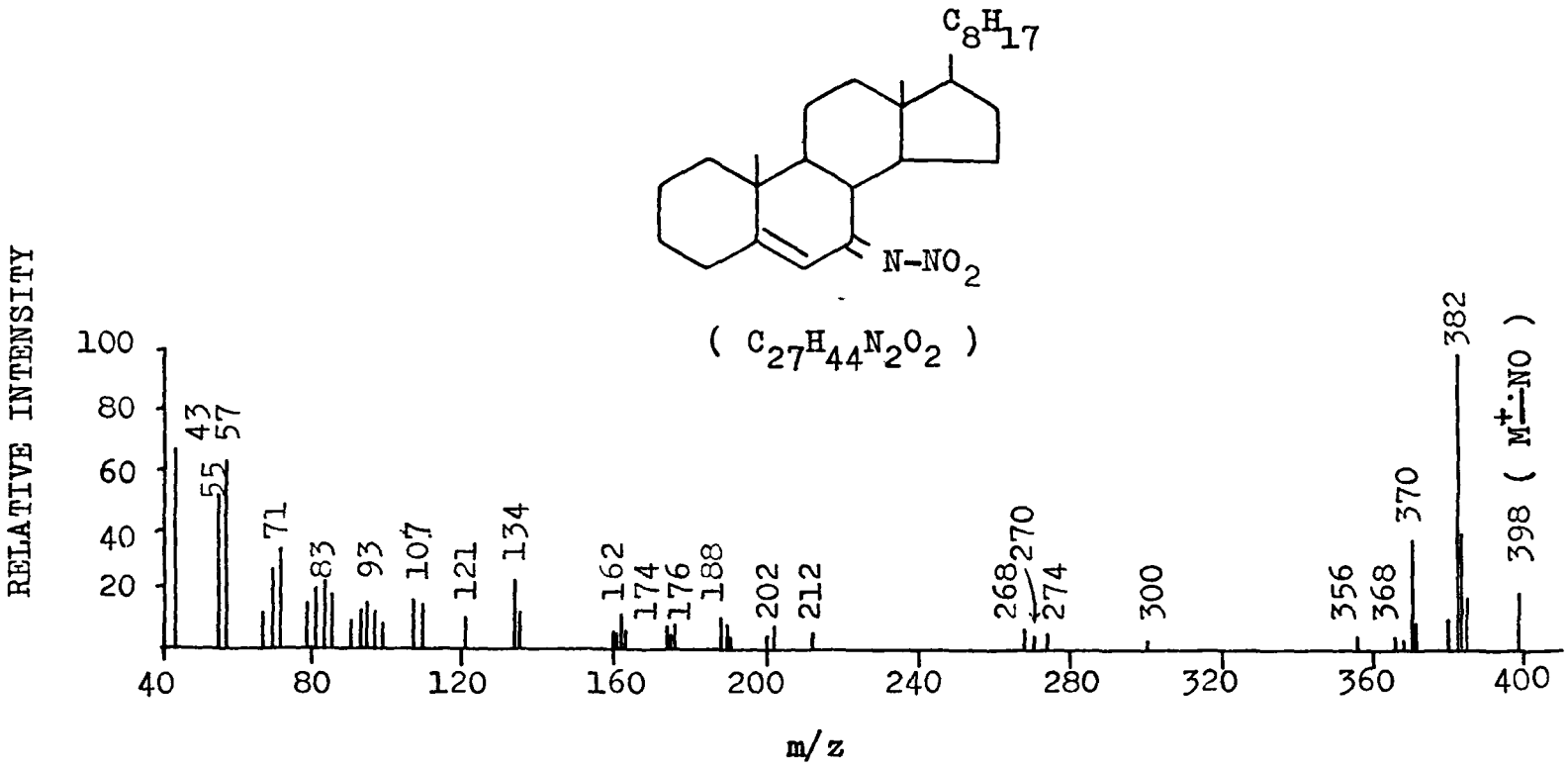
The ion m/z 382 constituting the base peak of the spectrum may be shown to arise by the loss of a molecule of acetic acid and NO_2 from the molecular ion.



(LIV') m/z 428 m/z 382

The mass spectrum of the nitrimine (LIV) after the ion m/z 382 follows the same fragmentation pattern as (CLXIII).

The mass spectrum of 6-nitrimino-3α,5-cyclo-5α-cholestane (CXXIII) (Figure 6) resembled those of the (CLXIII) and (CLIV). It gave the molecular ion peak at m/z 428 which was of very low intensity. The molecular ion peak was followed by the fragment ions at m/z 398 (M^+-NO), 382 (M^+-NO_2), 368 (M^+-N.NO_2),


C_8H_{17}
N-NO_2
($C_{27}H_{44}N_2O_2$)
RELATIVE INTENSITY
100
80
60
40
20
43
55
57
71
83
93
107
121
134
162
174
176
188
202
212
268
270
274
300
356
368
370
382
398 (M^+-NO)
40
80
120
160
200
240
280
320
360
400
m/z

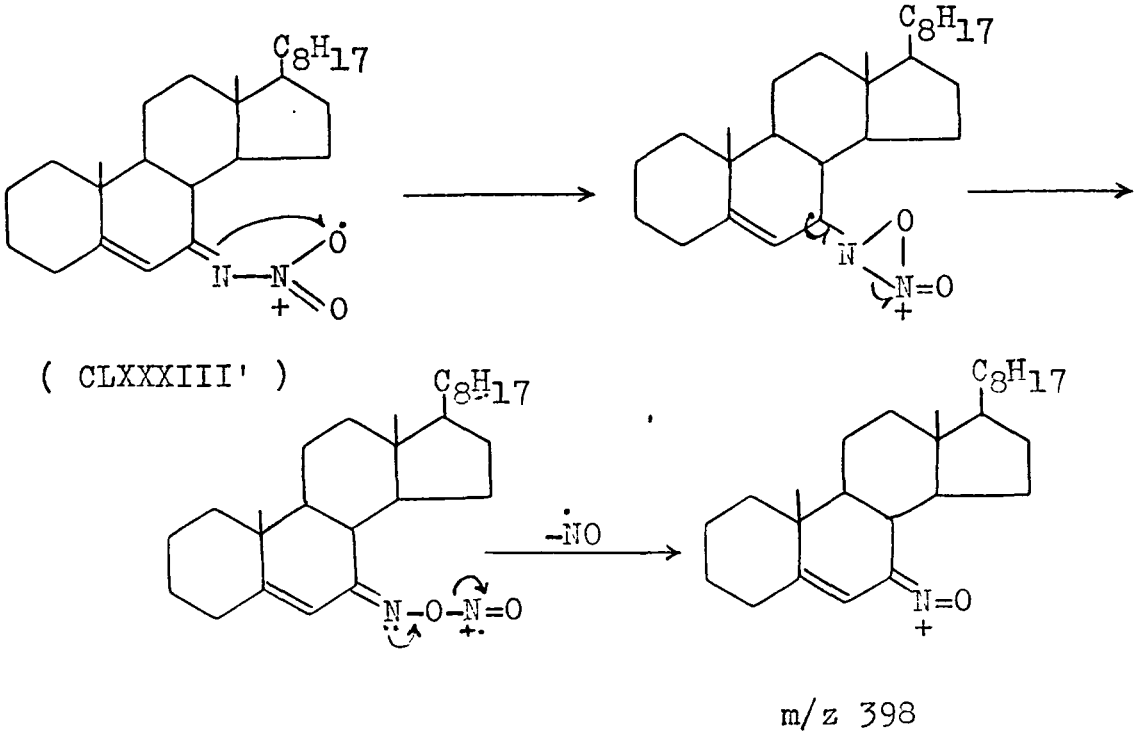
(Figure 7)

367 (382-CH_3), 366 (367-H), 340, 288, 252, 174, 162, 161, 159, 158, 147, 146, 145 and lower mass peaks.

The mass spectrum of 7-nitriminocholest-5-ene (CLXXXIII) (Figure 7) showed no molecular ion peak. The highest mass peak was observed at m/z 398 due to the initial loss of nitric oxide (NO) from the molecular ion. The other fragment ions were observed at m/z 383, 382, 368, 366, 270, 242, 202, 188, 176, 174, 162, 134 and lower mass peaks. The genesis of some of these ions has been shown in the following schemes.

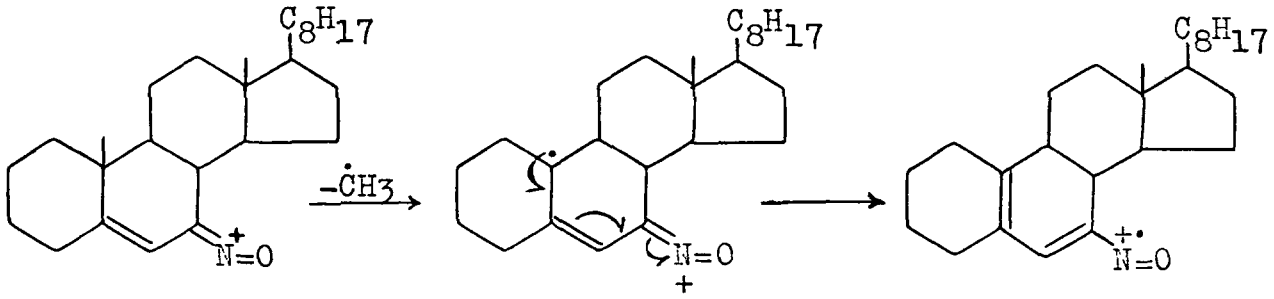
m/z 398

The ions m/z 398, constituting the highest mass peak of the spectrum, may be shown to arise by the initial loss of nitric oxide (NO) from the molecular ion.



m/z 398

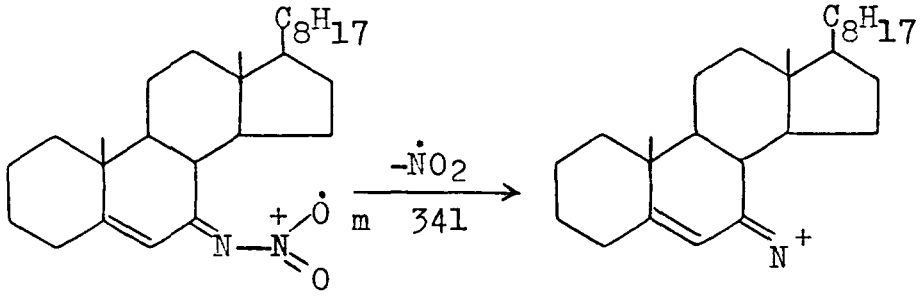
m/z 383 (m/z 398-CH_3)



m/z 398 m/z 383

m/z 382

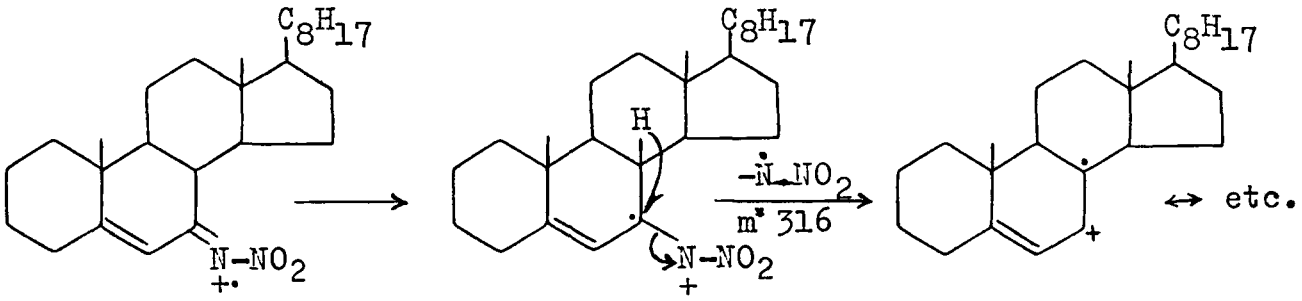
The ion m/z 382, constituting the base peak of the spectrum arises by the loss of NO_2 from the molecular ion.



(CLXXIII') m/z 382

m/z 368

This ion probably arises by the loss of $N-NO_2$ from the molecular ion to give a hydrocarbon fragment.



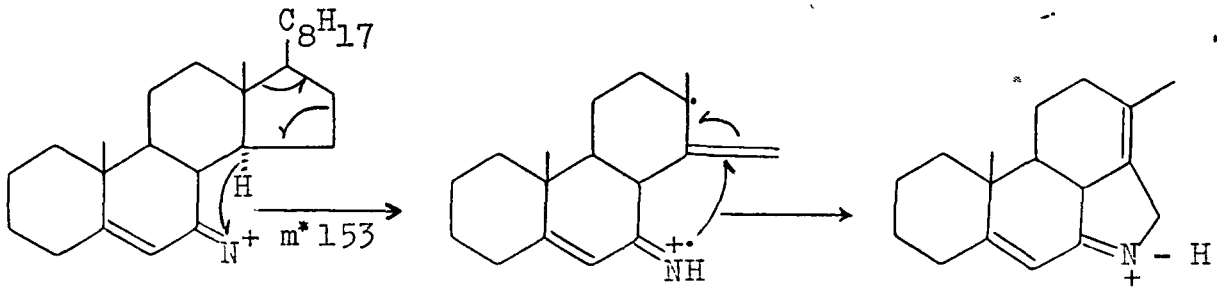
(CLXXXIII') m/z 368

m/z 270

This ion may be shown to arise by the loss of the side chain from the ion m/z 383.

m/z 242

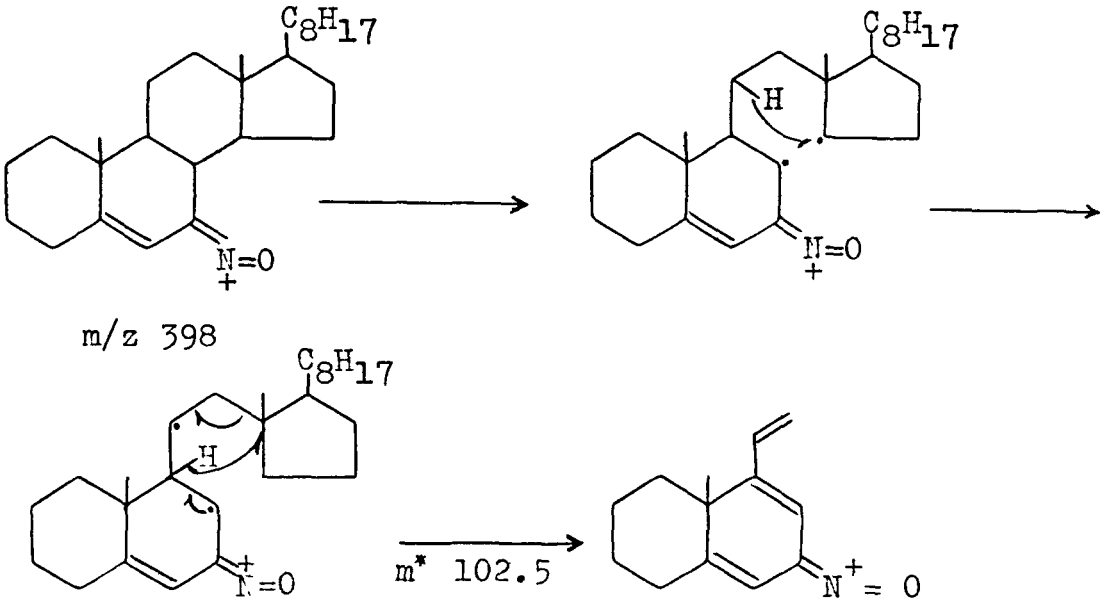
The ion m/z 242 arises most probably by the loss of side chain along with a part of ring D from the ion m/z 382, as shown below.



m/z 382 m/z 242

m/z 202 ($C_{13}H_{16}NO$)

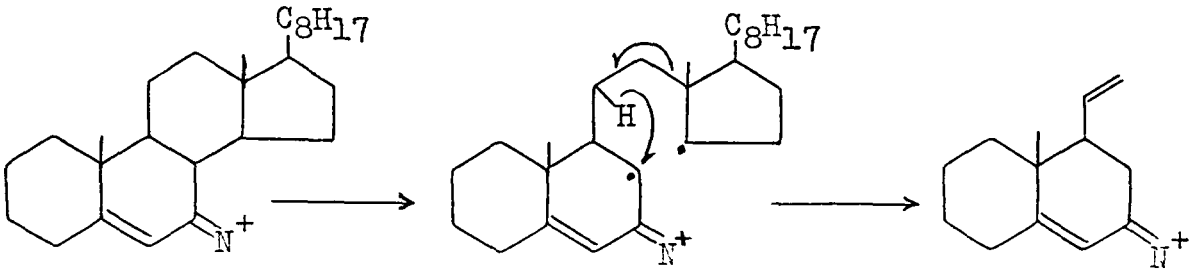
The genesis of the ion m/z 202 can be shown according to the following scheme.



m/z 202 ($C_{13}H_{16}NO$)

m/z 188 ($C_{13}H_{18}N$)

This ion may be shown to arise by the following sequence

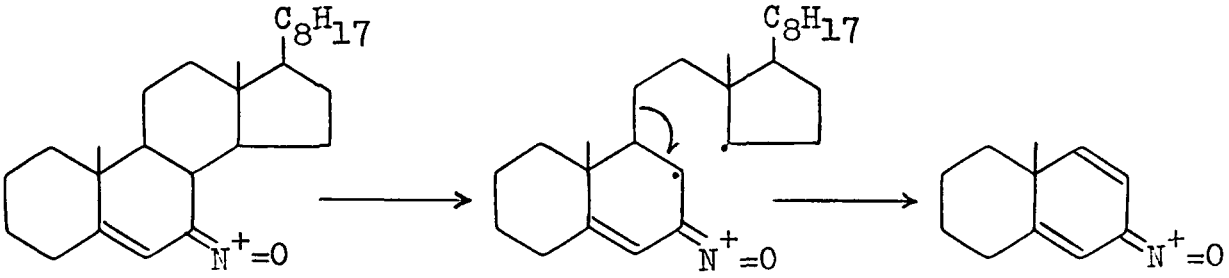


m/z 382

m/z 188 ($C_{13}H_{18}N$)

m/z 176 ($C_{11}H_{14}NO$)

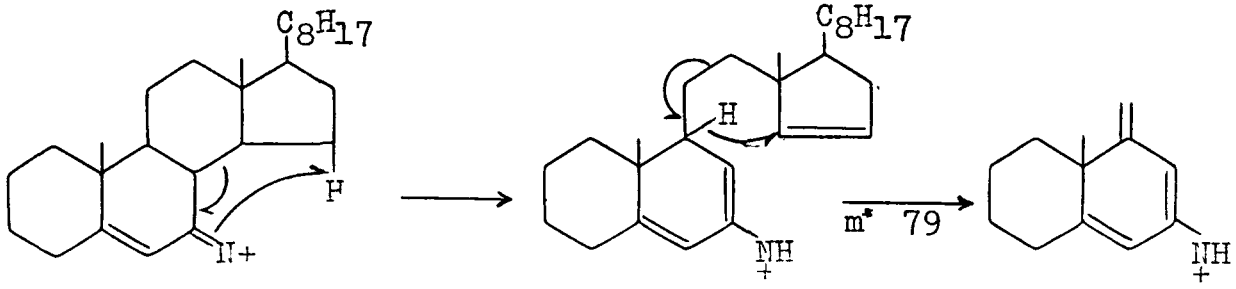
This ion may arise by the loss of rings C and D along with the side chain from the ion m/z 398.



m/z 398 m/z 176 ($C_{11}H_{14}NO$)

m/z 174 ($C_{12}H_{16}N$)

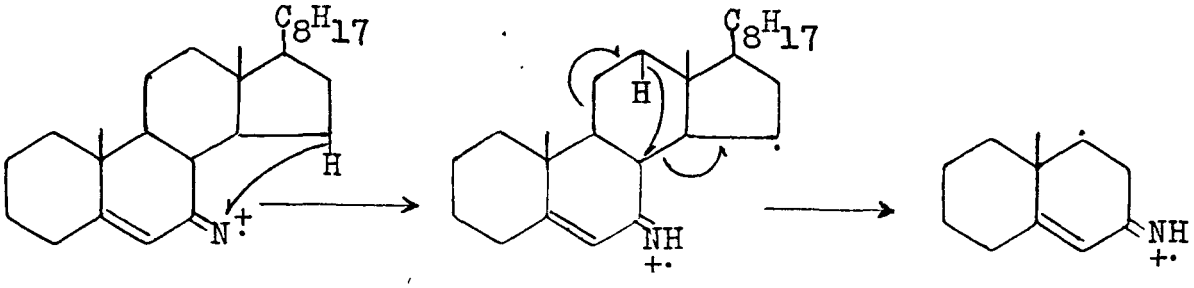
The ion m/z 174 may be shown to arise from the ion m/z 382 as follows:



m/z 382 m/z 174 ($C_{12}H_{16}N$)

m/z 162 ($C_{11}H_{16}N$)

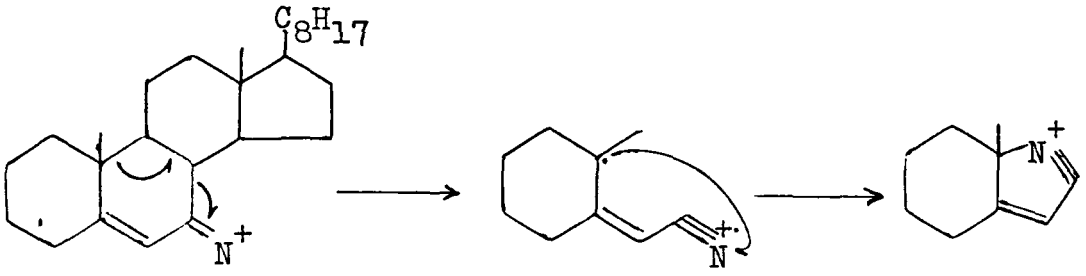
This ion can be shown to arise by the following sequence from the ion m/z 382.



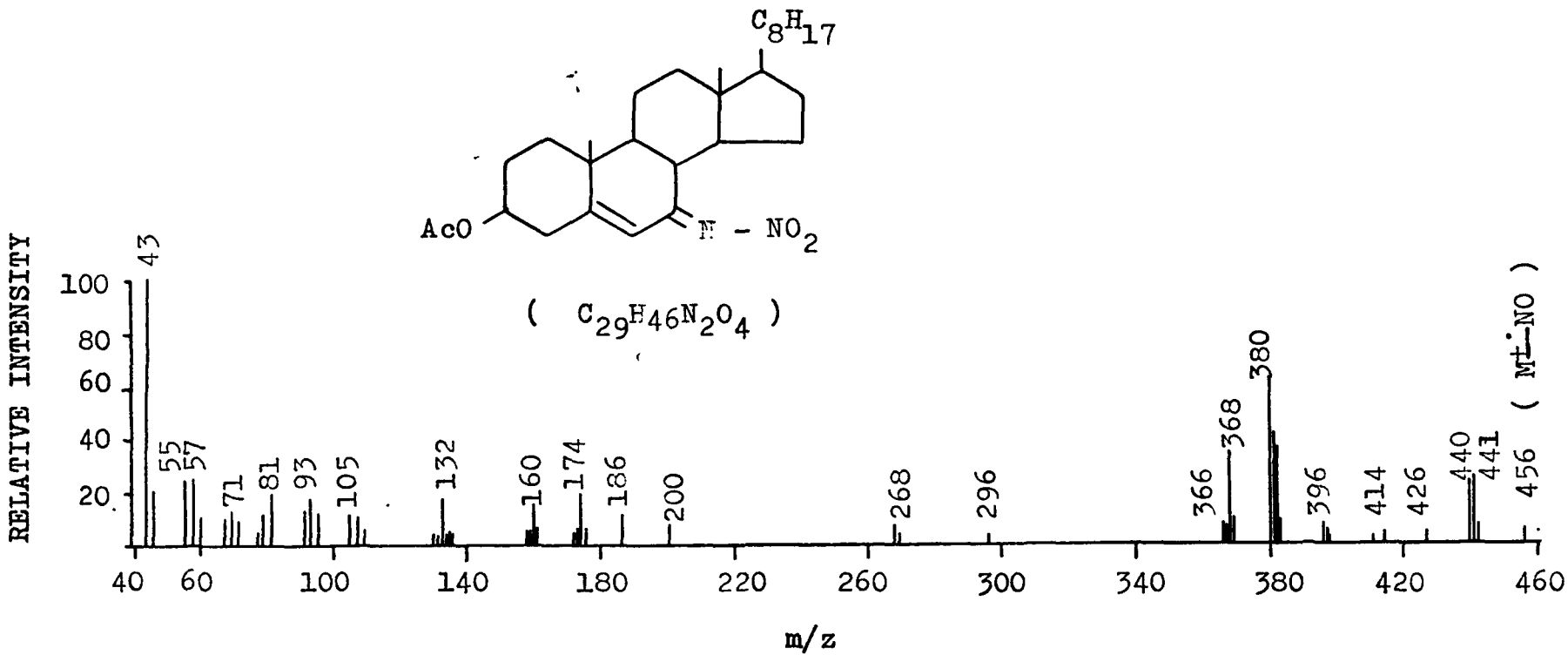
m/z 382 m/z 162 ($C_{11}H_{16}N$)

m/z 134 ($C_9H_{12}N$)

The ion m/z 134, arising most probably from ring A and part of ring B as a nitrile species can be shown to be formed accroding to the following scheme.



m/z 382 m/z 134 ($C_9H_{12}N$)

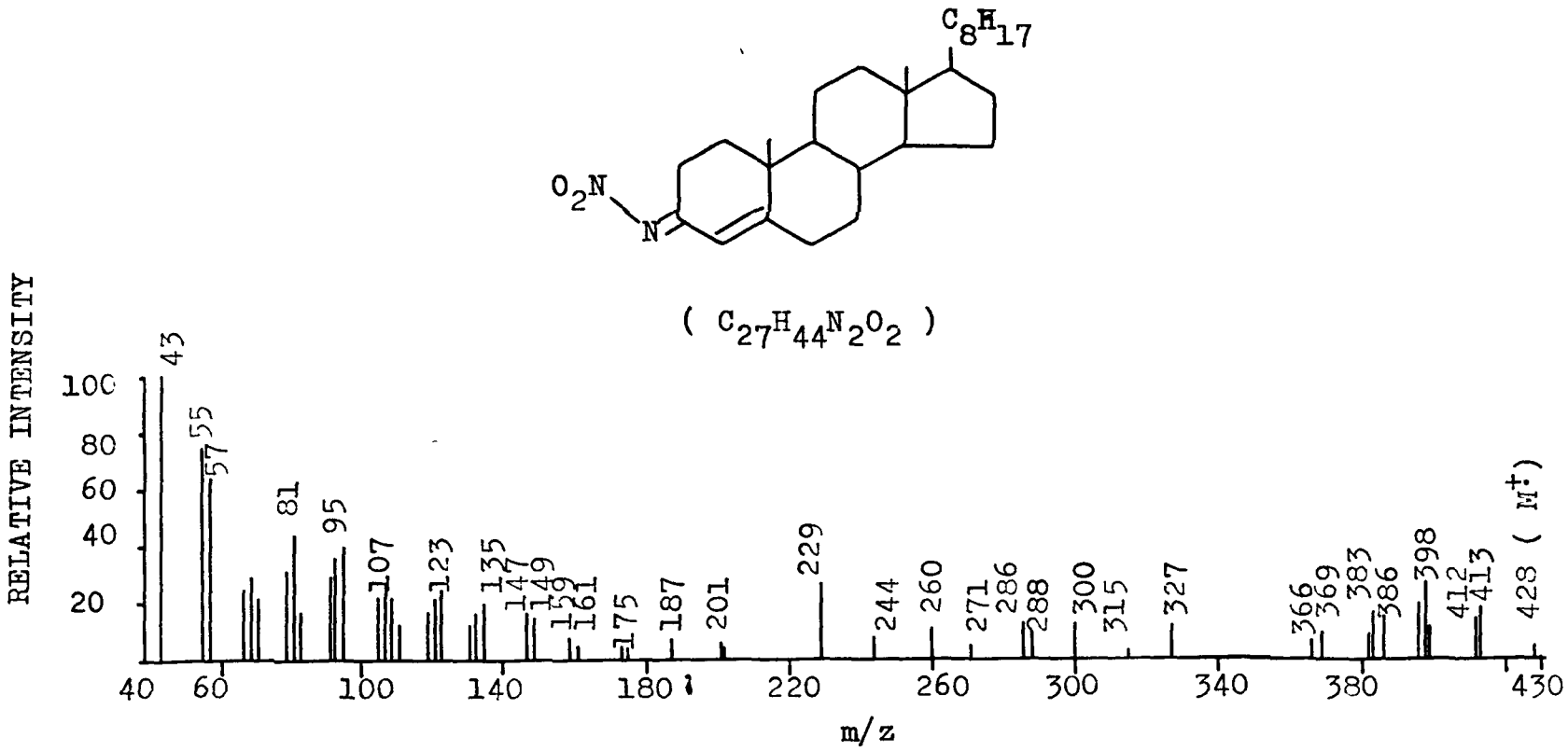

C_8H_{17}
AcO
NO_2
($C_{29}H_{46}N_2O_4$)
RELATIVE INTENSITY
100
80
60
40
20
43
55
57
71
81
93
105
132
160
174
186
200
268
296
366
368
380
396
414
426
440
441
456
(M^+-NO)
40
60
100
140
180
220
260
300
340
380
420
460
m/z

(Figure 8)

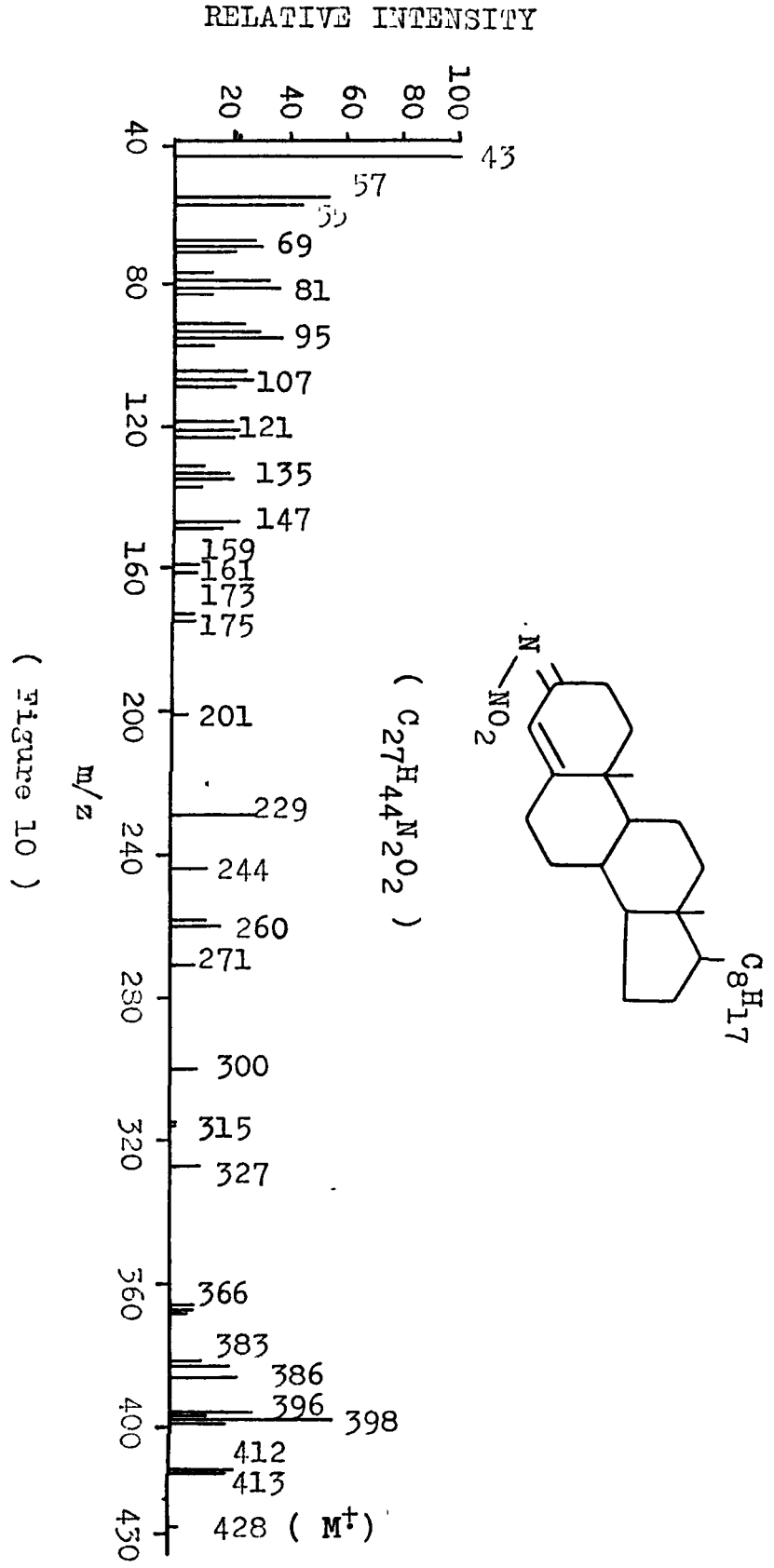
The mass spectrum of 7-nitriminocholest-5-en-3β-yl acetate (LV) (Figure 8) was quite similar to that of (CLXXXIII). The highest mass peak was observed at m/z 456 after the initial loss of nitric oxide from the molecular ion (m/z 486). The other fragment ions were obtained at m/z 381, 380, 368, 366, 268, 240, 200, 186, 174, 172, 160, 132 and lower mass peaks. It is evident from these ions that most of them arise after the loss of a molecule of acetic acid from the molecular ion and a difference of two mass units is therefore observed in the fragment ions obtained from (LV) and those from the unsubstituted nitrimine (CLXXXIII).

The mass spectra of anti-3-nitriminocholest-4-ene (CLXXVI) (Figure 9) and syn-3-nitriminocholest-4-ene (CLXXVII) (Figure 10) were measured in order to see how these geometrical isomers differ from each other in the fragmentation pattern. It was, however, found that the two spectra were quite similar, differing only in respect of the relative intensities of some of the fragment ion peaks.

The molecular ion peak for both the nitrimines (CLXXVI) and (CLXXVII) was observed at m/z 428 and it was followed by the fragment ions at m/z 413, 412, 398, 397, 396, 383, 382, 368, 367, 327, 315, 300, 288, 259, 247, 244, 229, 187, 175, 173, 161, 159 and lower mass peaks.


C_8H_{17}
O_2N
N
($C_{27}H_{44}N_2O_2$)
RELATIVE INTENSITY
100
80
60
40
20
43
55
57
81
95
107
123
135
147
149
159
161
175
187
201
229
244
260
271
286
288
300
315
327
366
369
383
386
398
412
413
428 (M^+)
40
60
100
140
180
220
260
300
340
380
430
m/z

(Figure 9)


RELATIVE INTENSITY
20
40
60
80
100
40
80
120
160
200
240
280
320
360
400
450
m/z
43
57
69
81
95
107
121
135
147
159
161
173
175
201
229
244
260
271
300
315
327
366
383
386
396
398
412
413
428 (M+)
(C27H44N2O2)
N
NO2
C8H17

(Figure 10)

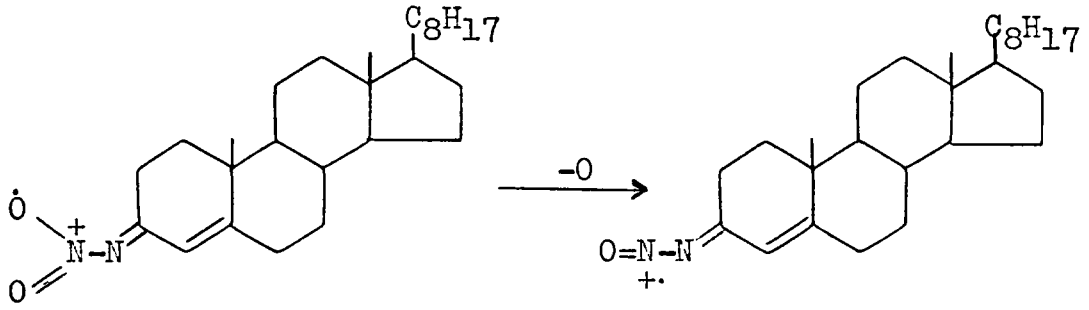
The genesis of some of the fragment ions and the differences observed in the relative intensity of the fragment in the spectra of the two nitrimines have been discussed in the following schemes.

m/z 413

The ion m/z 413 may arise from the molecular ion by the loss of a methyl radical.

m/z 412

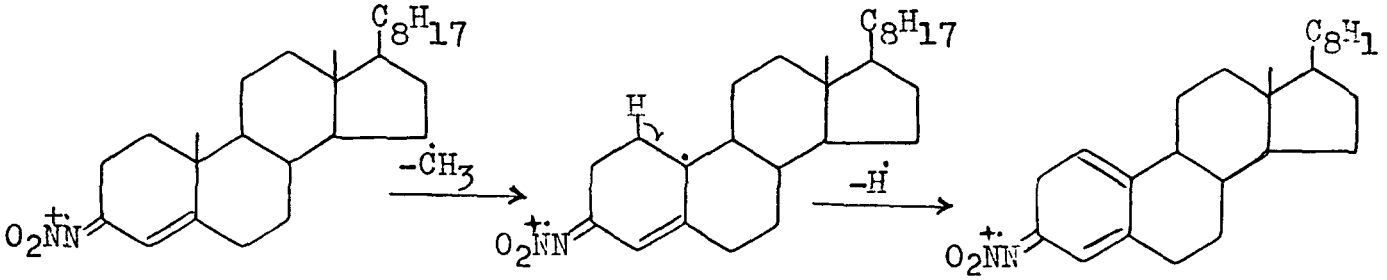
This ion may be shown to arise by the loss of an oxygen from the nitro group of the nitrimine function.



(CLXXVI')
(CLXXVII')

m/z 412

Alternatively, the ion m/z 412 can also arise by the loss of a hydrogen from the ion m/z 413.

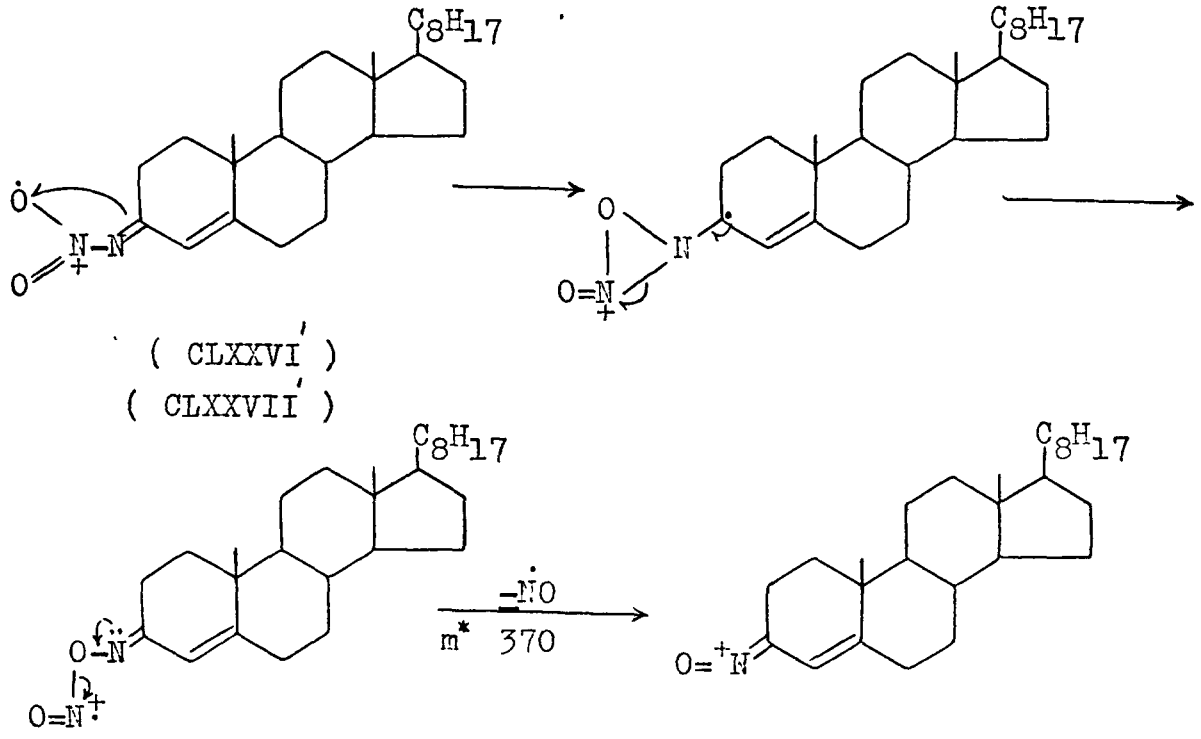


(CLXXVI') m/z 413 m/z 412

(CLXXVII')

m/z 398

The ion m/z 398 may be shown to arise by the loss of nitric oxide from the molecular ion.



(CLXXVI')

(CLXXVII')

m/z 398

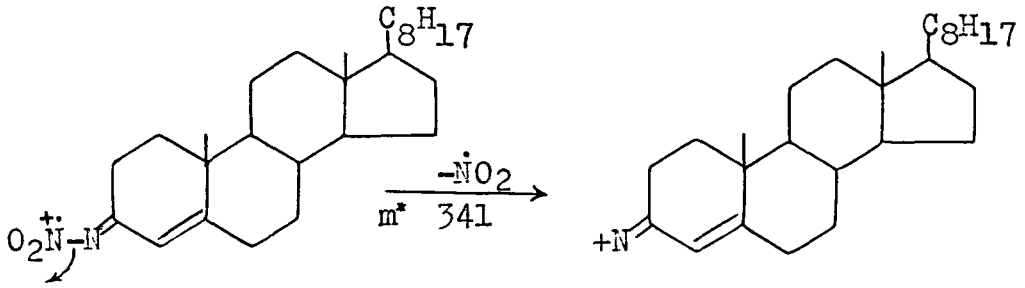
The relatively high intensity of the fragment ion m/z 398 in the syn-nitrimine (CLXXVII) as compared to the anti one (CLXXVI) can be explained on the basis of the steric strain which may facilitate the loss of NO.

m/z 383

This ion may arise by the loss of a methyl group from the ion m/z 398.

m/z 382

The ion m/z 382 arises by the loss of NO_2 from the molecular ion.

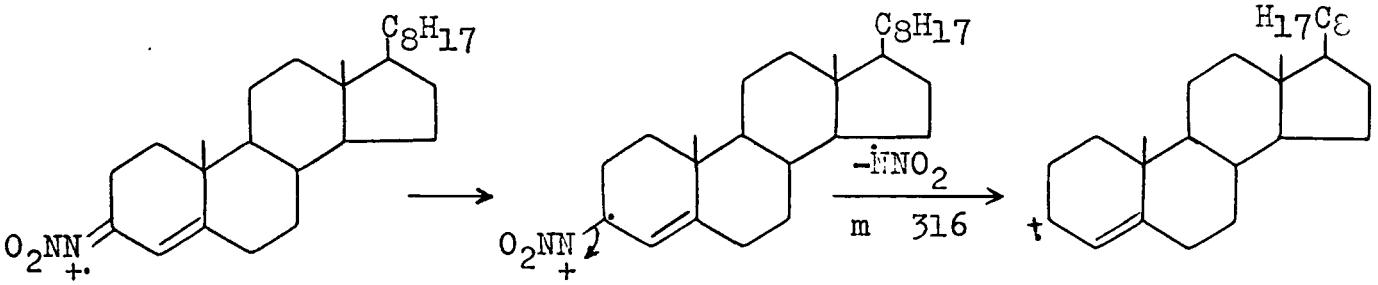


(CLXXVI')
(CLXXVII')

m/z 382

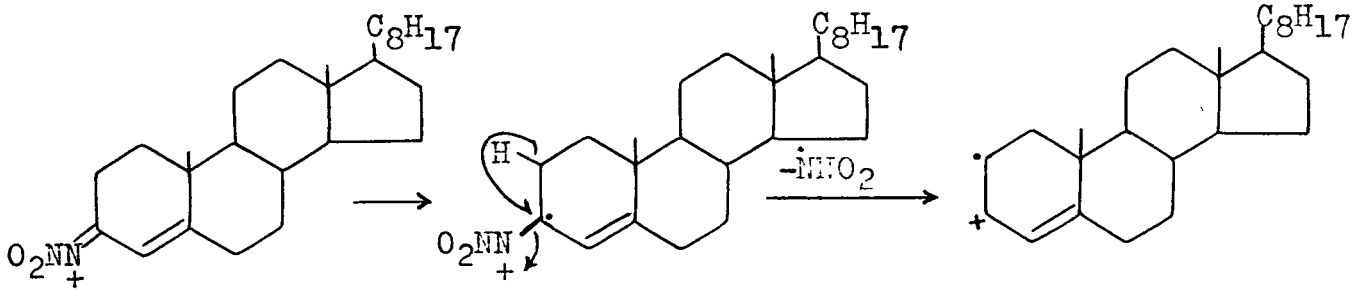
m/z 368

The ion m/z 368 can be shown to arise by the loss of $\dot{N}NO_2$ from the molecular ion to give a hydrocarbon fragment.



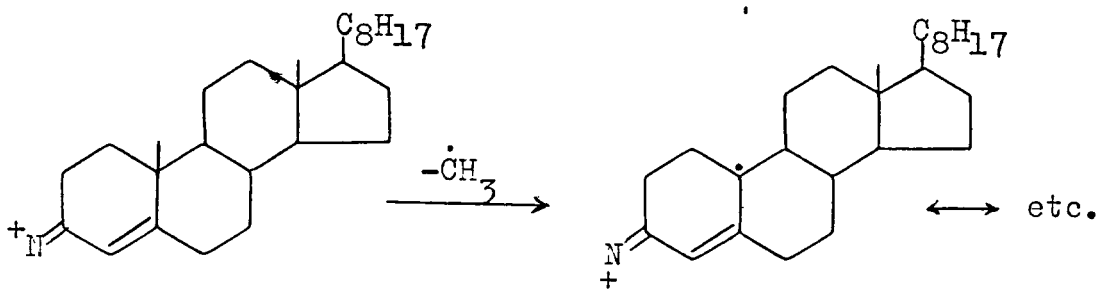
(CLXXVI')
(CLXXVII')

OR



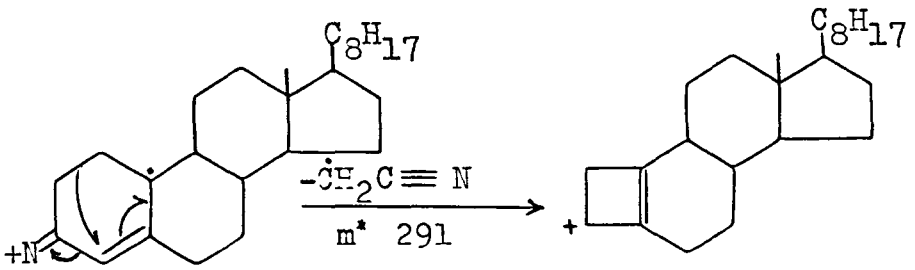
m/z 367

This ion arises most probably by the loss of a methyl group from the ion m/z 382



m/z 327

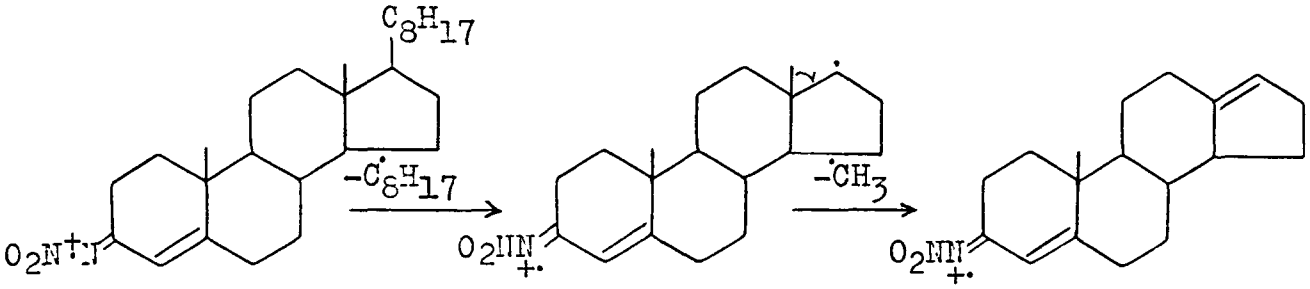
The ion m/z 327 may arise by the loss of a nitrile species ($CH_2C\equiv N$) from the ion m/z 367 according to the following scheme.



m/z 367 m/z 327 ($C_{24}H_{39}$)

m/z 315 and m/z 300

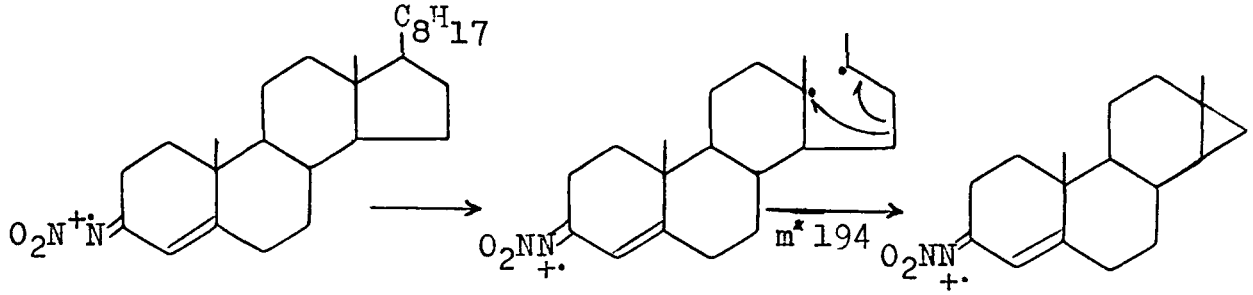
The ion m/z 315 arises most probably by the loss of side chain from the molecular ion. Further loss of a methyl group can account for the ion m/z 300.



(CLXXVI')
(CLXXVII') m/z 315 m/z 300

m/z 288

This ion can be shown to arise by the loss of side chain along with a part of ring D from the molecular ion.

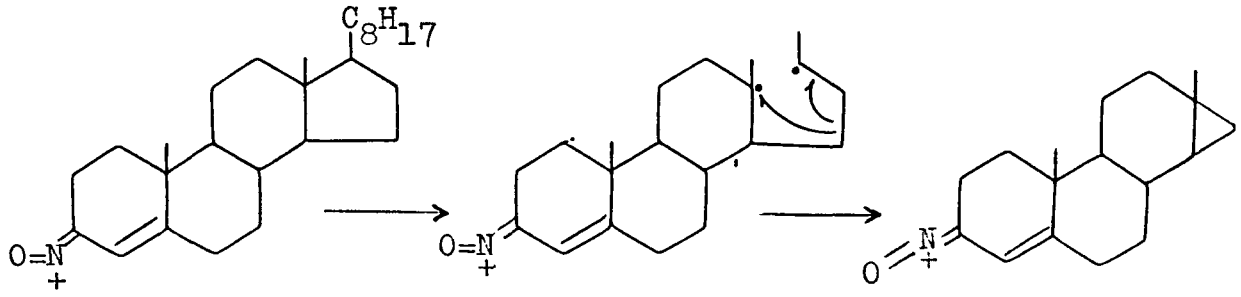


(CLXXVI′)
(CLXXVII′)

m/z 288

m/z 258

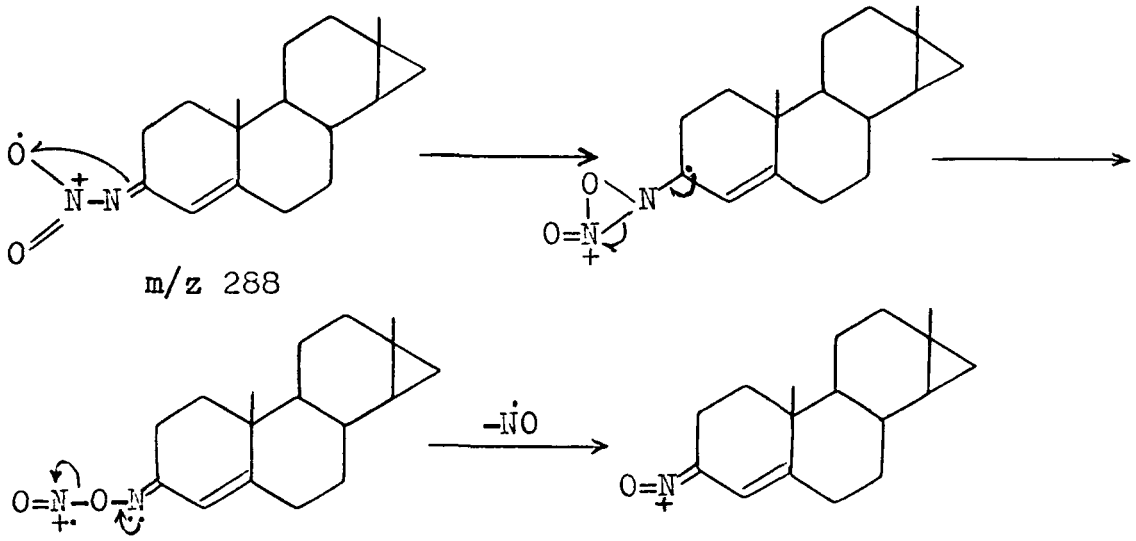
The ion m/z 258 may arise from the ion m/z 398 by the loss of side chain and a part of the ring D as shown below.



m/z 398

m/z 258

Alternatively, this ion can also arise by the loss of nitric oxide from the ion m/z 288.

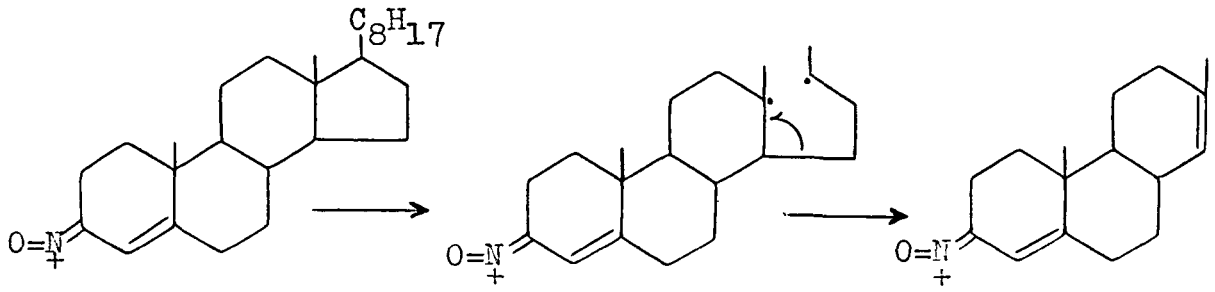


m/z 288

m/z 258

m/z 244

This ion can be accounted for by the loss of the side claim along with the ring D from the ion m/z 398 according to the following scheme.

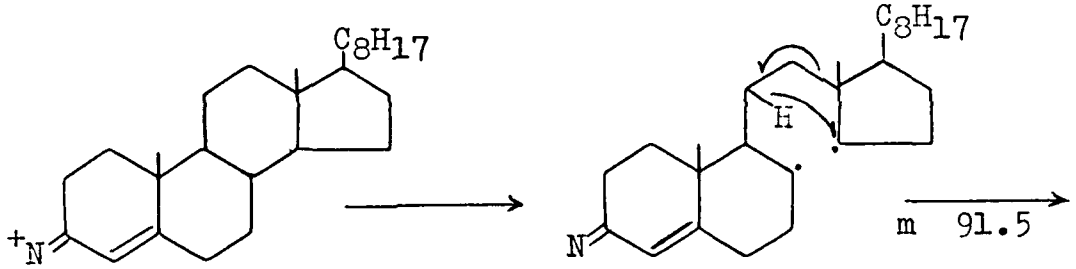


m/z 398

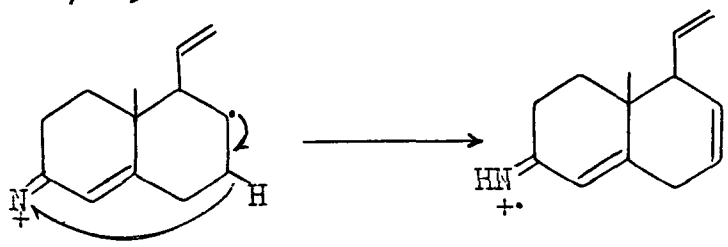
m/z 244

m/z 187 ($C_{13}H_{17}N$)

The ion m/z 187, comprising of rings A,B and part of ring C, can be shown to arise from the ion m/z 382 according to the following sequence.



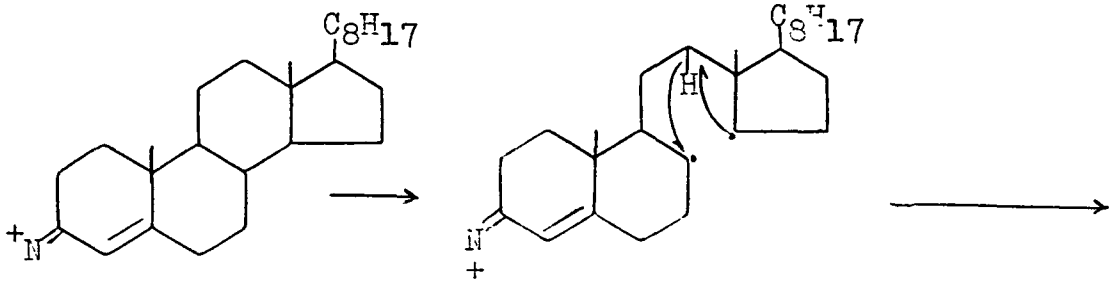
m/z 382

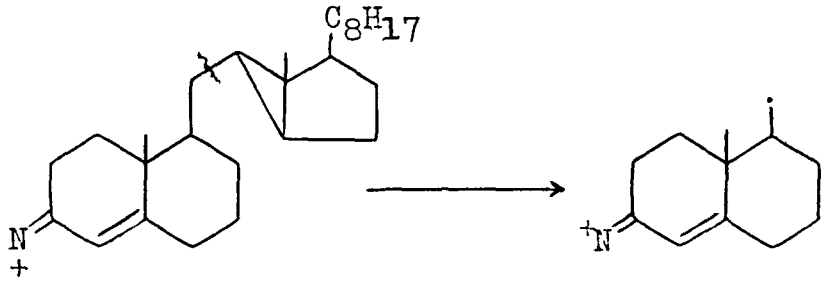


m/z 187 ($C_{13}H_{17}N$)

m/z 175 ($C_{12}H_{17}N$)

The ion m/z 175 can be shown to arise from the ion m/z 382 according to the following scheme.

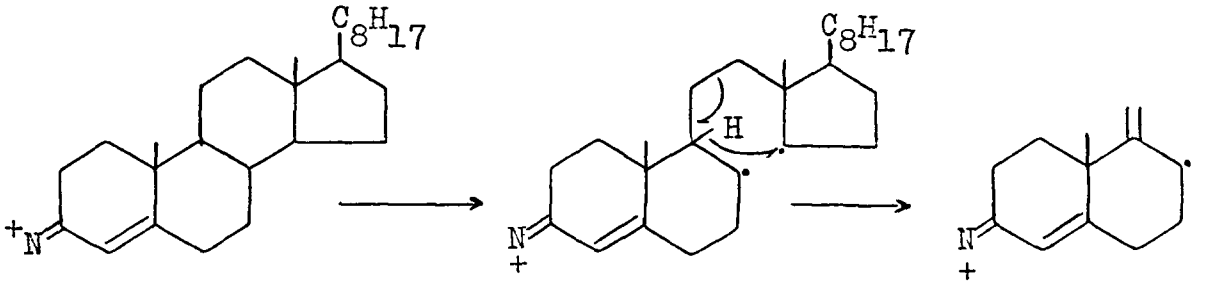




m/z 173 ($C_{12}H_{15}N$)

m/z 175 ($C_{12}H_{17}N$)

The genesis of the ion m/z 173 can be shown according to the following scheme.

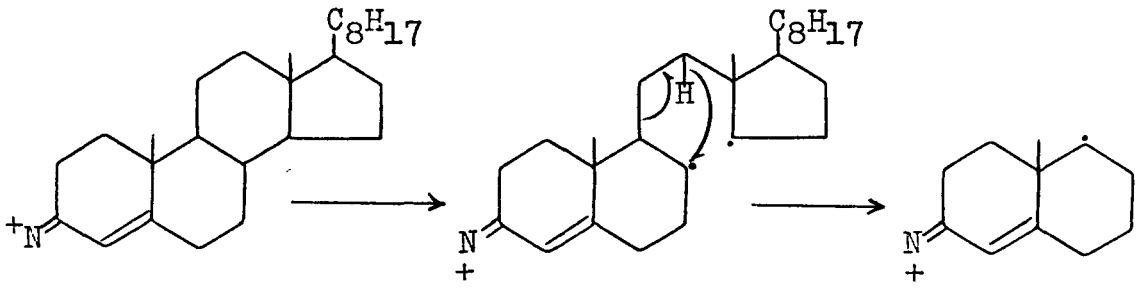


m/z 382

m/z 173 ($C_{12}H_{15}N$)

m/z 161 ($C_{11}H_{15}N$)

The ion m/z 161 can be shown to arise from the ion m/z 382 as follows.



m/z 382 m/z 161 ($C_{11}H_{15}N$)

From the present study of the C-nitro and N-nitro compounds, it became evident that in both the classes the loss of nitro group was responsible for the base peak in most of the cases. The initial loss of nitro group from the molecular ion was attributed to the fact that the nitro group is not a favourable charge-stabilizing centre. In most of the cases the fragmentation occurred after the loss of either NO or NO_2 from the molecular ion.

The spectra were, however, helpful and useful. The spectra of the nitro compounds can also be correlated with those of the oximes and the tosylhydrazones to some extent, especially after the loss of NO and NO_2 from the molecular ion.

E X P E R I M E N T A L

PART - ONE

All melting points are uncorrected. IR spectra were determined in nujol with a Perkin-Elmer 621 and Pye Unicam Sp3 100 spectrophotometers. NMR spectra were run in $CDCl_3$ on a Varian A60D instrument with TMS as internal standard. Mass spectra were measured on a GC-MS JMS D300 mass spectrometer using direct insertion technique at a source temperature of 250°C. Thin layer chromatographic plates were coated with silica gel G and sprayed with 20% aqueous perchloric acid. Light petroleum refers to a fraction of b.p. 60-80°. NMR values are given in ppm(s = singlet, d = doublet, t = triplet, br = broad, umc = unresolved multiplet centred at ; mc = multiplet centred at). IR values are given in cm^{-1} (s = strong, m = medium, w = weak, br = broad).

Cholest-5-en-3β-yl chloride (CCXXXII)

Freshly purified thionyl chloride (40 ml) was added to cholesterol (50 g) at room temperature. A vigorous reaction ensued with the evolution of gaseous products. When the reaction slackened, the reaction mixture was gently heated at a temperature of 50-60° on a water bath for one hour, and then poured on crushed ice with stirring. The yellow solid thus obtained was filtered under suction, washed several times with water and dried. Recrystallization from acetone gave cholest-

5-en-3β-yl chloride (38 g), m.p. 94-95° (lit.[156] m.p. 96-97°).

Cholest-5-ene (CCI)

Cholest-5-en-3β-yl chloride (10 g) was dissolved in warm amyl alcohol (230 ml) and sodium metal (20 g) was added to the solution with continuous stirring over a period of eight hours. The reaction mixture was warmed occasionally. When all the sodium metal was dissolved, the reaction mixture was poured into water, acidified with hydrochloric acid and then allowed to stand overnight. A white crystalline solid thus obtained was filtered under suction and washed thoroughly with water and air dried. The crude material was recrystallized from acetone to provide cholest-5-ene (8.3 g), m.p. 94° (lit.[121] m.p. 95°).

6-Nitrocholest-5-ene (CCL)

A suspension of finely powdered cholest-5-ene (6 g) in glacial acetic acid (50 ml) was vigorously stirred at room temperature and treated with nitric acid (15 ml; d, 1.5), followed by addition of sodium nitrite (3 g) over a period of one hour. The reaction mixture was poured into cold water and the yellow solid mass thus obtained was extracted with ether. The ethereal layer was washed successively with water, sodium bicarbonate solution (5%) and again with water and dried over anhydrous sodium sulphate. Removal of the solvent provided the desired compound as an oil which was crystallized from

ethanol to give 6-nitrocholest-5-ene as leaflets (4.5 g), m.p. 119-120° (lit.[152] m.p. 120-121°).

6-Oxo-5α-cholestane (CLXIV)

6-Nitrocholest-5-ene (6 g) was dissolved in warm glacial acetic acid (120 ml) and zinc dust (12 g) was gradually added with shaking over a period of thirty minutes. The reaction mixture was heated under reflux for four hours and water (12 ml) was added now and then during the course of reaction. After the completion of the reaction, the unreacted zinc powder was removed by filteration and the filtrate was diluted with water. 6-Oxo-5α-cholestane crystallized out as thin plates which was recrystallized from ethanol (3.5 g), m.p. 96-98° (lit.[100] m.p. 98-100°).

6-Oximino-5α-cholestane (CLXII)

6-oxo-5α-cholestane (3 g), hydroxylamine hydrochloride (3 g) and sodium acetate trihydrate (4.5 g) were dissolved in ethanol (180 ml) and the mixture was heated under reflux for two hours. The excess of the solvent was removed under reduced pressure and the residue was diluted with an excess of cold water. The crude oxime thus obtained was filtered under suction, washed with cold water and air dried. Recrystallization of the crude product from ethanol gave 6-oximino-5α-cholestane (2.7 g), m.p. 198-200° (lit.[99] m.p. 200-202°).

$\nu_{max.}$ 3260 m(NOH), 1670 m(C=N) cm^{-1}; δ 9.8 s(NO<u>H</u>, exchangeable with D_2O), 0.93, 0.83 and 0.68 (methyl protons).

<u>Nitrosation of 6-Oximino-5α-cholestane (CLXII):6-Nitrimino-5α-cholestane (CLXIII) and 6-oxo-5α-cholestane (CLXIV)</u>

6-Oximino-5α-cholestane (CLXII) (2 g) was dissolved in ether (100 ml) and to this was added a solution of sodium nitrite (2 g dissolved in 10 ml water). The mixture was cooled and taken in a separating funnel. Cold 2N sulphuric acid (20 ml) was added to the separating funnel and the funnel was immediately stoppered, rapidly inverted and vented. The mixture was shaken several times and the aqueous layer was withdrawn and discarded. The ether layer was transferred to an Erlenmeyer flask and allowed to react at room temperature for five hours. The ethereal solution was then washed successively with water, sodium bicarbonate solution (5%) and again with water and dried over anhydrous sodium sulphate. Evaporation of the solvent gave an oil which was chromatographed over silica gel (40 g). Each fraction of 25 ml was collected. Elution with light petroleum-ether (40:1) gave the nitrimine (CLXIII) which was recrystallized in methanol (1.4 g), m.p. 85°. $\nu_{max.}$ 1640 m(C=N), 1570 s($\nu_{as}NO_2$) and 1320 s($\nu_{s}NO_2$) cm^{-1}; δ 2.7 m(C_7-<u>H</u>$_2$), 0.95, 0.86 and 0.7 (methyl protons).

Analysis Found : C, 75.5; H, 10.6; N, 6.7%

$C_{27}H_{46}N_2O_2$ requires : C, 75.4; H, 10.7; N, 6.5%.

Further elution with light petroleum-ether (20:1) furnished the ketone (CLXIV), recrystallized from ethanol (0.5 g), m.p. and m.m.p. 98°.

Acid Hydrolysis of (CLXIII):6-Oxo-5α-cholestane (CLXIV)

The nitrimine (CLXIII) (0.5 g) was dissolved in methanol (50 ml) and dil. hydrochloric acid (10 ml) was added to it. The reaction mixture was heated on a water bath for one hour. The excess of the solvent was removed and the reaction mixture was allowed to attain room temperature when the ketone (CLXIV) started crystallizing out. It was filtered under suction and recrystallized from ethanol to give pure 6-oxo-5α-cholestane (CLXIV) (0.4 g) m.p. and m.m.p. 98° (lit.[100] m.p. 98°).

6-Nitrocholest-5-en-3β-yl chloride (CCLV)

To a well stirred mixture of cholest-5-en-3β-yl chloride (12 g), glacial acetic acid (80 ml) and nitric acid (25 ml; d, 1.5) at temperature below 20°, was added sodium nitrite (3 g) gradually over a period of two hours. After complete addition of sodium nitrite, the mixture was stirred for about one hour. Ice cold water was added and the yellowish solid thus obtained was filtered under suction and air dried. Recrystallization from methanol gave the desired 6-nitrocholest-5-en-3β-yl chloride as needles (8.3 g), m.p. 151-152° (lit.[153] m.p. 153°).

6-Oxo-5α-cholestan-3β-yl chloride (CLXIX)

To a solution of 6-nitrocholest-5-en-3β-yl chloride (12 g) in hot glacial acetic acid (240 ml), zinc dust (24 g) was added gradually in small portions with shaking. The suspension was heated under reflux for four hours and water (24 ml) was added at regular intervals during the course of the reaction. The hot solution was filtered to remove the unreacted zinc and the filtrate was diluted with an excess of ice cold water. The organic matter was extracted with ether and the ethereal solution was washed successively with water, sodium bicarbonate solution (5%) and again with water and dried over anhydrous sodium sulphate. Evaporation of the solvent gave an oil which was crystallized in methanol to give the ketone (8.7 g), m.p. 128-129° (lit.[102] m.p. 129-130°).

6-Oximino-5α-cholestan-3β-yl chloride (CLXVII)

6-Oxo-5α-cholestan-3β-yl chloride (3 g), hydroxylamine hydrochloride (3 g) and sodium acetate trihydrate (7.5 g) were dissolved in ethanol (180 ml) and the reaction mixture was refluxed on a boiling water bath for two hours. Excess of the solvent was removed under reduced pressure and the residue was diluted with an excess of ice cold water. The crude oxime thus obtained was filtered under suction, washed with water and air dried. Recrystallization from methanol gave the pure oxime (CLXVII) (2 g), m.p. 173-175° (lit.[101] m.p. 175°). $\nu_{max.}$

3280 m(NOH), 1665 m(C=N) and 750 m(C-Cl) cm^{-1}; δ 9.4 s(NOH, exchangeable with D_2O), 3.6 br($C_3\alpha\underline{H}$ $W\frac{1}{2}$ = 17 Hz), 0.9, 0.83 and 0.7 (methyl protons).

Nitrosation of 6-oximino-5α-cholestan-3β-yl chloride (CLXVII): 6-Nitrimino-5α-cholestan-3β-yl chloride (CLXVIII) and 6-oxo-5α-cholestan-3β-yl chloride (CLXIX)

6-Oximino-5α-cholestan-3β-yl chloride (CLXVII) (2 g) was dissolved in ether (100 ml) and to this was added a solution of sodium nitrite (2 g dissolved in 10 ml water). The mixture was cooled and taken in a separating funnel. Cold 2N sulphuric acid (20 ml) was added to the separating funnel and the funnel was immediately stoppered, rapidly inverted and vented. The mixture was shaken several times and the aqueous layer was withdrawn and discarded. The ether layer was transferred to an Erlenmeyer flask and allowed to react for five hours at room temperature. The ethereal solution was then washed successively with water, sodium bicarbonate solution (5%) and again with water and dried over anhydrous sodium sulphate. Evaporation of the solvent gave an oil which was chromatographed over silica gel (40 g). Each fraction of 25 ml was collected. Elution with light petroleum-ether (30:1) afforded the nitrimine (CLXVIII) which was recrystallized in methanol (1.2 g), m.p. 112°. $\nu_{max.}$ 1625 m(C=N), 1570 s($\nu_{as}NO_2$),

1315 s($\nu_s NO_2$) and 750 m(C-Cl) cm^{-1}; δ 3.63 m($C_3\alpha\underline{H}$, $W\frac{1}{2} = 22$ Hz), 0.95, 0.83 and 0.7 (methyl protons).

Analysis Found : C, 69.7; H, 9.5; N, 5.9%

$C_{27}H_{45}N_2O_2Cl$ requires : C, 69.8; H, 9.7; N, 6.0%

Further elution with light petroleum-ether (20:1) furnished the ketone (CLXIX) which was recrystallized from methanol (0.5 g), m.p. and m.m.p. 128°.

Hydrolysis of (CLXVIII):6-Oxo-5α-cholestan-3β-yl chloride(CLXIX)

A mixture of (CLXVIII) (0.5 g), methanol (50 ml) and dil. hydrochloric acid (10 ml) was heated under reflux for one hour. The volume of the solvent was reduced to half and the mixture was allowed to attain room temperature. The ketone (CLXIX) started separating out as fine crystals. It was filtered and recrystallized from methanol to give pure (CLXIX) (0.3 g), m.p. and m.m.p. 128° (lit.[102] m.p. 129-130°).

Cholest-5-en-3β-yl acetate (CCX)

A mixture of cholesterol (50 g), pyridine (75 ml) and acetic anhydride (50 ml) was heated on a water bath for two hours. The resulting brown solution was poured onto crushed ice-water mixture with stirring. The light brown solid thus obtained was filtered under suction, washed with water and air dried. The crude product on recrystallization from

acetone gave the pure acetate (45 g), m.p. 114-115° (lit.[122] m.p. 116°).

6-Nitrocholest-5-en-3β-yl acetate (CXLVIII)

Cholest-5-en-3β-yl acetate (5 g) was covered with nitric acid (100 ml; d, 1.42) and fuming nitric acid (25 ml; d, 1.52) was added to it. Sodium nitrite (5 g) was added to the suspension gradually over a period of one hour with continuous stirring. Slight external cooling was also affected during the course of the reaction, and the stirring was continued for additional two hours. The mixture was diluted with an excess of ice cold water when a yellow spongy mass separated on the surface and a green coloured solution was obtained. The whole mass was extracted with ether. The ethereal solution was washed successively with water, sodium bicarbonate solution (5%) and again with water and dried over anhydrous sodium sulphate. Evaporation of the solvent provided the nitro compound as an oil which was crystallized from methanol (3.5 g), m.p. 104° (lit.[121] m.p. 102-104°).

6-Oxo-5α-cholestan-3β-yl acetate (CLXXI)

6-Nitrocholest-5-en-3β-yl acetate (6 g) was dissolved in galcial acetic acid (250 ml) by warming the mixture and zinc dust (12 g) was added in small portions with shaking. The suspension was heated under reflux for four hours and water (12 ml) was added now and then during the course of the reaction.

The hot solution was filtered to remove zinc and diluted with an excess of ice cold water. The white precipitate thus obtained was taken in ether and the ethereal solution was washed successively with water, sodium bicarbonate solution (5%) and again with water and dried over anhydrous sodium sulphate. Evaporation of the ether gave an oil which was crystallized in methanol to give the ketone (4.2 g), m.p. 128-129° (lit.[104] m.p. 127-128°).

6-Oximino-5α-cholestan-3β-yl acetate (CLXX)

6-Oxo-5α-cholestan-3β-yl acetate (3 g) was dissolved in ethanol (180 ml) and hydroxylamine hydrochloride (3 g) and sodium acetate trihydrate (6 g) were added to it. The mixture was heated under reflux for two hours. The excess of the solvent was removed in vacuo and the residue was diluted with ice cold water. The crude oxime thus obtained was filtered under suction, washed with water and air dried. Recrystallization of the crude product from methanol gave pure oxime (CLXX) (2.2 g), m.p. 200° (lit.[103] m.p. 201°). $\nu_{max.}$ 3350 m(NOH), 1730 s($CH_3\overset{O}{\overset{\|}{C}}$-O), 1675 m(C=N) and 1245 s(acetate) cm^{-1}; δ 8.9 s(NO$\underline{H}$, exchangeable with D_2O), 4.6 br($C_3\alpha\underline{H}$, $W\frac{1}{2}$ = 16 Hz), 1.97 s($C\underline{H}_3COO$), 0.93, 0.83 and 0.7 (methyl protons).

Nitrosation of 6-oximino-5α-cholestan-3β-yl acetate (CLXX):-6-Nitrimino-5α-cholestan-3β-yl acetate (LIV) and 6-oxo-5α-cholestan-3β-yl acetate (CLXXI)

A separatory funnel was charged with a cold mixture of 6-oximino-5α-cholestan-3β-yl acetate (CLXX) (2 g) in ether (100 ml) and a solution of sodium nitrite (2 g in 10 ml water). Cold 2N sulphuric acid (20 ml) was added and the funnel was immediately stoppered, rapidly inverted and vented. The mixture was shaken several times and the aqueous layer was withdrawn and discarded. The ether layer was transferred to an Erlenmeyer flask and allowed to stand at room temperature for five hours. The solution was then worked up, dried over anhydrous sodium sulphate, evaporated and chromatographed over silica gel (40 g). Each fraction of 25 ml was collected. Elution with light petroleum-ether (40:1) furnished the nitrimine (LIV), recrystallized from methanol (1.4 g), m.p.135° $\nu_{max.}$ 1720 s(CH_3-$\overset{O}{\overset{\|}{C}}$-O), 1630 m(C=N), 1570 s($\nu_{as}NO_2$), 1320 s($\nu_s NO_2$) and 1240 s(acetate) cm^{-1}; δ 4.6 m($C_3\alpha\underline{H}$, $W\frac{1}{2}$ = 17 Hz), 1.97 s($C\underline{H}_3COO$), 0.93, 0.83 and 0.7 (methyl protons).

Analysis Found : C, 71.1; H, 9.7; N, 5.6%

$C_{29}H_{48}N_2O_4$ requires : C, 71.3; H, 9.8; N, 5.7%

Elution with light petroleum-ether (20:1) gave the ketone (CLXXI) which was recrystallized from methanol (0.4 g), m.p. and m.m.p. 127°.

Acid hydrolysis of (LIV):6-Oxo-5α-cholestan-3β-yl acetate(CLXXI)

6-Nitrimino-5α-cholestan-3β-yl acetate (LIV) (0.5 g) was dissolved in methanol (50 ml) and dil. hydrochloric acid (10 ml) was added to it. The mixture was heated under reflux for one hour. The solvent was removed under reduced pressure and the reaction mixture was allowed to cool. The solid compound which separated out was filtered and recrystallized from methanol to give 6-oxo-5α-cholestan-3β-yl acetate (CLXXI) (0.35 g), m.p. and m.m.p. 126° (lit.[104] m.p. 127-128°).

6-Oxo-3α-5-cyclo-5α-cholestane (CLXXIV)

A mixture of 6-oxo-5α-cholestan-3β-yl chloride (CLXIX) (5 g), methanol (75 ml) and potassium hydroxide pellets (3.7 g) was refluxed on a boiling water bath for one hour. The reaction mixture was poured into water and the organic matter was extracted with ether. The ethereal solution was washed successively with water, dilute hydrochloric acid, sodium bicarbonate solution (5%) and again with water and dried over anhydrous sodium sulphate. Evaporation of the solvent gave an oil which was crystallized in methanol to give the cycloketone (CLXXIV) (3.5 g), m.p. 96-97° (lit.[106] m.p. 97°).

6-Oximino-3α,5-cyclo-5α-cholestane (CLXXII)

To a solution of 6-oxo-3α,5-cyclo-5α-cholestane (CLXXIV) (2 g) in ethanol (120 ml) was added hydroxylamine hydrochloride

(2 g) and sodium acetate trihydrate (3 g) and the mixture was heated under reflux for two hours. The excess of the solvent was removed under reduced pressure and the residue was diluted with cold water. The crude oxime thus obtained was filtered under suction, washed with cold water and air dried. Recrystallization from methanol provided the pure oxime (CLXXII) (1.7 g), m.p. 143° (lit.[105] m.p. 143-144°). $\nu_{max.}$ 3390 m(NOH), 3010 w(cyclopropane), 1650 m(C=N) cm^{-1}, δ 8.8 br(NO<u>H</u>, exchangeable with D_2O), 0.94, 0.9, 0.83, 0.68 (methyl protons) and 0.5-0.6 (cyclopropane protons).

<u>Nitrosation of 6-oximino-3α,5-cyclo-5α-cholestane (CLXXII): 6-Nitrimino-3α,5-cyclo-5α-cholestane (CLXXIII) and 6-oxo-3α, 5-cyclo-5α-cholestane (CLXXIV)</u>

A solution of 6-oximino-3α,5-cyclo-5α-cholestane (2 g) in ether (100 ml) and sodium nitrite (2 g in 10 ml water) was taken in a separating funnel and cold 2N sulphuric acid (20 ml) was added to it. The funnel was immediately stoppered, rapidly inverted and vented. The mixture was shaken several times and the aqueous layer was withdrawn and discarded. The ethereal solution was transferred to an Erlenmeyer flask and allowed to react at ambient temperature for five hours. The solution was then washed successively with water, sodium bicarbonate solution (5%) and again with water and dried over anhydrous sodium sulphate. Evaporation of the solvent gave

an oil which on column chromatography over silica gel (40 g) (light petroleum-ether 50:1 as eluent) afforded the nitrimine (CLXXIII) which was recrystallized from methanol (1.1 g), m.p. 80°. $\nu_{max.}$ 3020 w(cyclopropane), 1620 m(C=N), 1575 s($\nu_{as}NO_2$) and 1310 s(ν_sNO_2) cm^{-1}; δ 1.0, 0.93, 0.83, 0.71 (methyl protons) and 0.56 (cyclopropane protons).

Analysis Found : C, 75.5; H, 10.4; N, 6.3%

$C_{27}H_{44}N_2O_2$ requires : C, 75.7; H, 10.3; Nm 6.6% .

Further elution with light petroleum-ether (30:1) gave the ketone (CLXXIV), recrystallized from methanol (0.6 g), m.p. and m.m.p. 96°.

Mild hydrolysis of (CLXXIII):6-Oxo-3α,5-cyclo-5α-cholestane (CLXXIV)

The nitrimine (CLXXIII) (0.5 g) was dissolved in methanol (50 ml) and was treated with dil. hydrochloric acid (10 ml) at room temperature for two hours. On allowing the reaction mixture to cool, a solid mass separated out which was filtered and recrystallized from methanol to give the ketone (CLXXIV) (0.32 g), m.p. and m.m.p. 96° (lit.[106] m.p. 97°).

5α,6β-Dibromocholestan-3β-ol

To a solution of cholesterol (14 g) in ether (100 ml) was added gradually bromine solution (5 ml bromine dissolved in

100 ml glacial acetic acid containing 1 g of anhydrous sodium acetate) with stirring. The solution turned yellow and promptly set to a stiff paste of dibromide. The mixture was cooled and stirred with a glass rod for five minutes to ensure complete crystallization. The product was then filtered under suction and washed with a cold ether-acetic acid (3:7) mixture until the filtrate was completely colourless. The white dibromide was air dried (15 g), m.p. 112-113° (lit.[110] m.p.113°).

3-Oxo-5α,6β-dibromocholestane

5α,6β-Dibromocholestan-3β-ol (10 g) was suspended in acetone (300 ml) in a three necked flask fitted with a stirrer and a dropping funnel. The suspension was stirred for five minutes and Jones' reagent (15 ml) was then added dropwise from a dropping funnel in the course of fifteen minutes. The temperature of the reaction mixture during oxidation was maintained between 0-5° by external cooling. After the addition was complete, stirring was continued for additional fifteen minutes and cold water (200 ml) was then added. The product thus obtained was filtered under suction, washed thoroughly with water and air dried to give the dibromoketone (8.5 g), m.p. 73-75° (lit.[110] m.p. 75°).

3-Oxocholest-5-ene

3-Oxo-5α,6β-dibromocholestane (5 g) was dissolved in ether (100 ml) and glacial acetic acid (2.5 ml) was added.

Zinc dust (7.5 g) was then added in small portions during thirty minutes with continuous shaking. After the complete addition, the ether layer containing suspended zinc dust was filtered, washed successively with water, sodium bicarbonate solution (5%) and again with water and dried over anhydrous sodium sulphate. Removal of the solvent provided an oil which was crystallized from methanol to give 3-oxocholest-5-ene (3 g), m.p. 126° (lit.[110] m.p. 129°).

3-Oxocholest-4-ene (CLXXIX)

A solution of 3-oxocholest-5-ene (3 g) in ethanol (30 ml) containing oxalic acid (0.4 g) was heated under reflux for fifteen minutes. The reaction mixture was poured into cold water and extracted with ether. The ethereal solution was washed successively with water, sodium bicarbonate solution (5%) and again with water and dried over anhydrous sodium sulphate. The oily residue, obtained after the evaporation of the solvent, was crystallized from ethanol to give the ketone (CLXXIX) (1.2 g), m.p. 80° (lit.[110] m.p. 81-82°).

3-Oximinocholest-4-ene (CLXXV)

A mixture of 3-oxocholest-4-ene (2 g), ethanol (120 ml), hydroxylamine hydrochloride (3 g) and sodium acetate trihydrate (4.5 g) was refluxed on a boiling water bath for three hours. The excess of the solvent was removed under reduced pressure

and the residue was diluted with ice cold water. The crude oxime thus obtained was filtered under suction, washed thoroughly with cold water and air dried. No attempt was made to recrystallize the oxime (CLXXV) (1.5 g), m.p. 150° (lit.[107] m.p. 155°) $\nu_{max.}$ 3290 m(NOH), 1640 m(C=N) and 1615 w(C=C) cm^{-1}; δ 7.9 s(NO<u>H</u>, exchangeable with D_2O), 6.5 s(C_4-vinylic <u>H</u>), 1.1, 0.9, 0.8 and 0.71 (methyl protons).

<u>Nitrosation of 3-oximinocholest-4-ene (CLXXV):Anti-3-nitriminocholest-4-ene (CLXXVI), syn-3-nitriminocholest-4-ene (CLXXVII) 3-oximino-5-nitrocholestane (CLXXVIII) and 3-oxocholest-4-ene (CLXXIX)</u>

3-Oximinocholest-4-ene (CLXXV) (4 g) was dissolved in ether (200 ml) and to this was added a solution of sodium nitrite (4 g dissolved in 40 ml water). The solution was transferred to a separating funnel and cold 2N sulphuric acid (40 ml) was added to it. The reaction mixture was shaken several times and the aqueous layer was withdrawn and discarded. The ether layer was transferred to an Erlenmeyer flask and allowed to react at room temperature for six hours. The ethereal solution was then washed successively with water, sodium bicarbonate solution (5%) and again with water and dried over anhydrous sodium sulphate. Evaporation of the solvent and column chromatography over silica gel (80 g) (light petroleum-ether 40:1 as eluent) afforded the <u>anti</u>

nitrimine (CLXXVI), recrystallized from methanol (0.8 g), m.p. 105°. $\nu_{max.}$ 1640 m(C=N), 1620 m(C=C), 1565 s($\nu_{as}NO_2$) and 1320 s(ν_sNO_2) cm^{-1}; δ 5.8 s(C_4-vinylic H), 1.15, 0.9, 0.83 and 0.67 (methyl protons).

Analysis Found : C, 75.5; H, 10.1; N, 6.4%

$C_{27}H_{44}N_2O_2$ requires : C, 75.7; H, 10.3; N, 6.6%

Continued elution with light petroleum-ether (40:1) afforded the syn nitrimine (CLXXVII) which was recrystallized from methanol (0.9 g), m.p. 142°. $\nu_{max.}$ 1660 m(C=N), 1560 s($\nu_{as}NO_2$) and 1340 s(ν_sNO_2) cm^{-1}, δ 6.9 s(C_4-vinylic H), 1.03, 0.9, 0.83 and 0.67 (methyl protons).

Analysis Found : C, 75.8; H, 10.4; N, 6.5%

$C_{27}H_{44}N_2O_2$ requires : C, 75.7; H, 10.3; N, 6.6%

Elution with light petroleum-ether (30:1) gave 3-oximino-5α-nitrocholestane (CLXXVIII), recrystallized from methanol (0.5 g), m.p. 175°. $\nu_{max.}$ 3320 m(NOH), 1630 m(C=N), 1560 s($\nu_{as}NO_2$) and 1350 s(ν_sNO_2) cm^{-1}, δ 8.6 s(NOH, exchangeable with D_2O), 1.1, 0.93, 0.81 and 0.7 (methyl protons).

Analysis Found : C, 72.8; H, 10.4; N, 6.5%

$C_{27}H_{46}N_2O_3$ requires : C, 72.6; H, 10.4; N, 6.3%.

Further elution with light petroleum-ether (20:1) furnished the ketone (CLXXIX), recrystallized in methanol (0.8 g), m.p. and m.m.p. 79°.

Hydrolysis of (CLXXVI) and (CLXXVII):3-Oxocholest-4-ene (CLXXIX)

The hydrolysis of anti- and syn- forms of 3-nitriminocholest-4-ene (CLXXVI) and (CLXXVII) respectively, (0.5 g each) was carried out as described earlier. The reaction mixture on evaporation of the solvent gave a solid which was filtered under suction and recrystallized from methanol to give (CLXXIX) (0.3 g), m.p. and m.m.p. 80° (lit.[110] m.p. 81-82°).

7-Oxocholest-5-ene (CLXXXIV)

A solution of t-butyl chromate [From t-butyl alcohol (60 ml), chromium trioxide (20 g), acetic acid (84 ml) and acetic anhydride (10 ml)] was added at 0°C to a solution of cholest-5-ene (8 g) in carbon tetrachloride (150 ml), acetic acid (30 ml) and acetic anhydride (10 ml). The contents were heated under reflux for five hours and then the reaction mixture was diluted with water. The organic layer was washed successively with water, sodium bicarbonate solution (5%) and again with water and dried over anhydrous sodium sulphate. Removal of the solvent under reduced pressure gave an oil which was crystallized from methanol to give the ketone (CLXXXIV) (3 g), m.p. 129° (lit.[112] m.p. 125-129°).

7-Oximinocholest-5-ene (CLXXXII)

7-Oxocholest-5-ene (CLXXXII) (2.5 g), hydroxylamine hydrochloride (3.5 g) and sodium acetate trihydrate (3.5 g)

were dissolved in ethanol (125 ml). The mixture was heated under reflux for three hours on a boiling water bath. The excess of the solvent was removed under reduced pressure and the residue was diluted with an excess of ice cold water. The crude oxime thus obtained was filtered under suction, washed with water and air dried. Recrystallization from methanol gave the pure oxime (CLXXXII) (1.8 g), m.p. 185° (lit.[111] m.p. 188-189°). $\nu_{max.}$ 3270 m(NOH), 1640 m(C=N) and 1610 m(C=C) cm^{-1}, δ 8.1 s(NO<u>H</u>, exchangeable with D_2O), 5.7 s(C_6-vinylic <u>H</u>), 1.1, 0.93, 0.8 and 0.71 (methyl protons).

<u>Nitrosation of 7-oximinocholest-5-ene (CLXXXII):7-Nitriminocholest-5-ene (CLXXXIII) and 7-oxocholest-5-ene (CLXXXIV)</u>

7-Oximinocholest-5-ene (CLXXXII) (2 g) was dissolved in ether (100 ml) and a solution of sodium nitrite (2 g in 10 ml water) was added to it. The solution was taken in a separating funnel and cold 2N sulphuric acid (20 ml) was added to the funnel. The separating funnel was stoppered, rapidly inverted and vented. The mixture was shaken several times and the aqueous layer was withdrawn and discarded. The ether layer was transferred to an Erlenmeyer falsk and allowed to react for five hours at room temperature. The ethereal solution was washed successively with water, sodium bicarbonate solution (5%) and again with water and dried over anhydrous sodium sulphate. Evaporation of the solvent gave an oil which was chromatographed over silica gel (40 g). Each fraction of 25 ml

was collected. Elution with light petroleum-ether (30:1) afforded the nitrimine (CLXXXIII) which was recrystallized from methanol (1.1 g), m.p. 68°. $\nu_{max.}$ 1660 m(C=N), 1620 m(C=C), 1565 s($\nu_{as}NO_2$) and 1320 s($\nu_{s}NO_2$) cm^{-1}, δ 5.6 s(C_6-vinylic H), 1.1, 0.91, 0.83 and 0.67 (methyl protons).

Analysis Found : C, 75.4; H, 10.5; N, 6.7%

$C_{27}H_{44}N_2O_2$ requires : C, 75.7; H, 10.3; N, 6.6%

Further elution with light petroleum-ether (20:1) gave the ketone (CLXXXIV), recrystallized from methanol (0.5 g), m.p. and m.m.p. 125°.

Hydrolysis of 7-nitriminocholest-5-ene(CLXXXIII):7-Oxocholest-5-ene (CLXXXIV)

The nitrimine (CLXXXIII) (0.5 g) was dissolved in methanol (50 ml) and dil. hydrochloric acid (10 ml) was added to it. The mixture was heated under reflux for one hour and the excess of the solvent was removed. A white crystalline solid separated out which was filtered under suction and recrystallized from methyl alcohol to give (CLXXXIV) (0.4 g), m.p. and m.m.p. 125° (lit.[112] m.p. 125-129°).

7-Oxocholest-5-en-3β-yl chloride (CLXXXVIII)

A solution of t-butyl chromate [From t-butyl alcohol (60 ml), chromium trioxide (20 g), acetic acid (84 ml) and acetic anhydride (10 ml)] was added at 0°C to a solution of

cholest-5-en-3β-yl chloride (8 g) in carbon tetrachloride (150 ml), acetic acid (30 ml) and acetic anhydride (10 ml). The contents were refluxed for five hours and then the reaction mixture was diluted with a large excess of water. The organic layer was washed successively with water, sodium bicarbonate solution (5%) and again with water and dried over anhydrous sodium sulphate. Evaporation of the carbon tetrachloride in vacuo furnished an oily residue which was crystallized in methanol to give the ketone (CLXXXVIII) (3.5 g), m.p. 144° (lit.[115] m.p. 144-145°).

7-Oximinocholest-5-en-3β-yl chloride (CLXXXVI)

7-Oxocholest-5-en-3β-yl chloride (CLXXXVIII) (3 g) was dissolved in ethanol (125 ml). Hydroxylamine hydrochloride (4 g) and sodium acetate trihydrate (4 g) were added to the above solution and the mixture was heated under reflux for three hours on a boiling water bath. The excess of the solvent was removed under reduced pressure and the residue was diluted with an excess of ice cold water. The crude oxime thus obtained was filtered under suction, washed with water and air dried. Recrystallization from methanol gave the oxime (CLXXXVI) (2.3 g), m.p. 195° (lit.[113] m.p. 197°). $\nu_{max.}$ 3290 m(NOH), 1645 m(C=N), 1620 m(C=C) and 730 m(C-Cl) cm^{-1}, δ 7.89 s(NO$\underline{H}$, exchangeable with D_2O), 5.76 s(C_6-vinylic $\underline{H}$), 3.55 m($C_3\alpha\underline{H}$, $W\frac{1}{2}$ = 17 Hz), 1.15, 0.91, 0.83 and 0.71 (methyl protons).

Nitrosation of 7-Oximinocholest-5-en-3β-yl chloride (CLXXXVI): 7-Nitriminocholest-5-en-3β-yl chloride (CLXXXVII) and 7-oxocholest-5-en-3β-yl chloride (CLXXXVIII)

A separatory funnel was charged with a cold solution of 7-oximinocholest-5-en-3β-yl chloride (CLXXXVI) (2 g) in ether (100 ml) and sodium nitrite (2 g dissolved in 10 ml water). Cold 2N sulphuric acid (20 ml) was added and the funnel was shaken several times. The aqueous layer was withdrawn and discarded. The ether layer was transferred to an Erlenmeyer flask and allowed to react at room temperature for five hours. The solution was then worked up, dried over anhydrous sodium sulphate and evaporated to give an oily residue. Column chromatography of the oil over silica gel (40 g) (light petroleum-ether 40:1 as eluent) afforded the nitrimine (CLXXXVII) which was recrystallized from methanol (1.4 g), m.p. 138°.

$\nu_{max.}$ 1640 m(C=N), 1600 m(C=C), 1565 s($\nu_{as}NO_2$), 1310 s($\nu_{s}NO_2$) and 735 m(C-Cl) cm^{-1}; δ 5.7 s(C_6-vinylic H), 3.5 m($C_3\alpha$-H, $W\frac{1}{2}$ = 20 Hz), 1.2, 0.9, 0.83 and 0.7 (methyl protons).

Analysis Found : C, 70.3; H, 9.1; N, 6.2%

$C_{27}H_{43}N_2O_2Cl$ requires : C, 70.1; H, 9.3; N, 6.1%

Further elution with light petroleum-ether (30:1) furnished the ketone(CLXXXVIII), recrystallized from methanol (0.4 g), m.p. and m.m.p. 144°.

Hydrolysis of (CLXXXVII): 7-Oxocholesta-3,5-diene (CLXXXIX)

A mixture of (CLXXXVII) (0.5 g), methanol (50 ml) and dil. hydrochloric acid (10 ml) was heated under reflux for one hour. On allowing the reaction mixture to cool, a white solid separated out which was filtered and recrystallized from methanol to give the dienone (CLXXXIX) (0.25 g) m.p. and m.m.p. 116° (lit.[114] m.p. 118°).

7-Oxocholest-5-en-3β-yl acetate (CXCI)

To a solution of cholest-5-en-3β-yl acetate (8 g) in carbon tetrachloride (150 ml), acetic acid (30 ml) and acetic anhydride (10 ml) was added at 0°C a solution of t-butyl chromate [From t-butyl alcohol (60 ml), chromium trioxide (20 g), acetic acid (84 ml) and acetic anhydride (10 ml)]. The mixture was heated under reflux for five hours and the reaction mixture was diluted with cold water. The organic layer was washed with water, sodium bicarbonate solution (5%) and again with water and dried over anhydrous sodium sulphate. Evaporation of the solvent under reduced pressure gave an oil which was crystallized from methanol to give the ketone (CXCI) (4 g), m.p. 162 (lit.[117] m.p. 164°).

7-Oximinocholest-5-en-3β-yl acetate (CXC)

7-Oxocholest-5-en-3β-yl acetate (CXCI) (3 g), hydroxylamine hydrochloride (4 g) and sodium acetate trihydrate (4 g) were

dissolved in ethanol (125 ml) and the mixture was heated under reflux for three hours on a boiling water bath. The excess of the solvent was removed under reduced pressure and the residue was diluted with cold water. The crude oxime thus obtained was filtered under suction, washed with water and air dried. Recrystallization from methanol gave the pure oxime (CXC) (2.5 g), m.p. 187° (lit.[116] m.p. 189°). $\nu_{max.}$ 3450 m(NOH), 1735 s(CH_3-C(=O)-O), 1630 m(C=N), 1600 m(C=C), 1275 s(acetate) and 1040 m(C-O) cm^{-1}; δ 8.3 s(NO<u>H</u>, exchangeable with D_2O), 5.68 s(C_6-vinylic <u>H</u>), 4.5 m($C_3\alpha$-<u>H</u>, $W\frac{1}{2}$ = 17 Hz), 2.18 s($C\underline{H}_3COO$), 1.2, 0.93, 0.8 and 0.7 (methyl protons).

<u>Nitrosation of 7-oximinocholest-5-en-3β-yl acetate (CXC): 7-Nitiminocholest-5-en-3β-yl acetate (LV) and 7-oxocholest-5-en-3β-yl acetate (CXCI)</u>

A solution of 7-oximinocholest-5-en-3β-yl acetate (CXCI) (2 g) in ether (100 ml) and sodium nitrite (2 g in 10 ml water) was taken in a separating funnel and cold 2N sulphuric acid (20 ml) was added to it. The mixture was shaken several times and the aqueous layer was withdrawn and discarded. The ether layer was transferred to an Erlenmeyer flask and allowed to react at room temperature for five hours. The ethereal solution was then washed successively with water, sodium bicarbonate solution (5%) and again with water and dried over anhydrous sodium sulphate. Evaporation of the solvent gave an oil

which was chromatographed over silica gel (40 g). Each fraction of 25 ml was collected. Elution with light petroleum-ether (30:1) afforded the nitrimine (LV) which was recrystallized from methanol (1.5 g), m.p. 155°. $\nu_{max.}$ 1730 s(CH_3-$\overset{O}{\overset{\|}{C}}$-O), 1640 m(C=N), 1600 m(C=C), 1570 s($\nu_{as}NO_2$), 1320 s($\nu_{s}NO_2$), 1240 m(acetate) and 1030 m(C-O) cm^{-1}; δ 5.6 s(C_6vinylic H), 4.6 m($C_3\alpha$H, $W\frac{1}{2}$ = 18 Hz), 1.97 s(CH_3COO), 1.2, 0.9, 0.81 and 0.73 (methyl protons).

Analysis Found : C, 71.5; H, 9.3; N, 5.9%

$C_{29}H_{46}N_2O_4$ requires : C, 71.6; H, 9.5; N, 5.8%

Further elution with light petroleum-ether (20:1) afforded the ketone (CXCI), recrystallized from methanol (0.3 g), m.p. and m.m.p. 162°.

7-Oxocholesta-3,5-diene (CLXXXIX)

To a solution of 7-oxocholest-5-en-3β-yl acetate (CXCI) in ethanol (100 ml) was added hydrochloric acid (5 ml; 12N) and the reaction mixture was heated under reflux for two hours. On allowing the reaction mixture to cool, the dienone (CLXXXIX) separated as plates which was filtered and recrystallized from ethanol (3.5 g), m.p. 115° (lit.[114] m.p. 118°).

6β-Hydroxy-5-bromo-5α-cholestan-3β-yl acetate

Cholest-5-en-3β-yl acetate (12 g) was dissolved in ether (200 ml) and to this was added at 0°C perchloric acid (1.6 ml)

and N-bromosuccinimide (9.6 g). The mixture was stirred at ambient temperature for two hours. The ethereal solution was then washed with water, sodium thiosulphate solution (5%) and again with water and dried over anhydrous sodium sulphate. Evaporation of the solvent gave an oil which was crystallized from light petroleum to give the bromohydrin (8 g), m.p. 160° (lit.[157] m.p. 162°).

6-Oxo-5-bromo-5α-cholestan-3β-yl acetate

To a suspension of 6β-hydroxy-5-bromo-5α-cholestan-3β-yl acetate (10 g) in acetone (300 ml), Jones' reagent (15 ml) was added gradually over a period of fifteen minutes. The reaction mixture was stirred at 5-10°C for two hours and was diluted with an excess of ice cold water. The α-bromoketone obtained as a white solid was filtered under suction, washed with cold water and air dried. Recrystallization from methanol gave pure α-bromoketone (8.5 g), m.p. 162-164° (lit.[158] m.p. 162°).

6-Oxocholest-4-en-3β-yl acetate

A mixture of 6-oxo-5-bromo-5α-cholestan-3β-yl acetate (5 g) and pyridine (50 ml) was heated under reflux for eight hours under anhydrous conditions. The reaction mixture was poured into cold water, acidified with dilute hydrochloric acid and extracted with ether. The ethereal solution was washed successively with water, sodium bicarbonate solution (5%) and again with water and

dried over anhydrous sodium sulphate. Removal of the solvent provided an oil which was crystallized in methanol to give the ketone (3.5 g), m.p. 106-108° (lit.[158] m.p. 110°).

3,6-Dioxo-5α-chloestane (CXCV)

A mixture of 6-oxocholest-4-en-3β-yl acetate (2 g), concentrated hydrochloric acid (2 ml) and ethanol (50 ml) was heated under reflux for one hour. Half of the alcohol was removed under reduced pressure when the dione started crystallizing out. The solid was filtered under suction and recrystallized from methanol (1.5 g), m.p. 166° (lit.[118] m.p. 169°).

3,6-Dioximino-5α-cholestane (CXCII)

3,6-Dioxo-5α-cholestane (CXCV) (2 g), hydroxylamine hydrochloride (4 g) and sodium acetate trihydrate (6 g) were taken in ethanol (120 ml) and the mixture was heated under reflux for three hours. The excess of alcohol was removed under reduced pressure and the residue was diluted with cold water. The white solid thus obtained was filtered under suction, washed with water and air dried. Recrystallization from methanol gave the dioxime (1.5 g), m.p. 210° (lit.[118] m.p. 202°). $\nu_{max.}$ 3320 m(NOH), 1640 m (C=N) cm^{-1} ; δ 8.6 br(2H, C_3 and C_6 NO<u>H</u>, exchangeable with D_2O), 0.93, 0.8, 0.71 and 0.67 (methyl protons).

Nitrosation of 3,6-dioximino-5α-cholestane (CXCII):3,6-Dinitrimino-5α-cholestane (CXCIII), 6-nitrimino-3-oxo-5α-cholestane (CXCIV) and 3,6-dioxo-5α-cholestane (CXCV)

3,6-Dioximino-5α-cholestane (CXCII) (2 g) was dissolved in ether (100 ml) and a solution of sodium nitrite (4 g in 20 ml water) was added to it. The mixture was cooled and transferred to a separating funnel. Cold 2N sulphuric acid (40 ml) was then added and the funnel was immediately stoppered, rapidly inverted and vented. The mixture was shaken several times and the aqueous layer was withdrawn and discarded. The ethereal layer was transferred to an Erlenmeyer flask and allowed to react at room temperature for six hours. After the completion of reaction, the ethereal solution was washed successivley with water, sodium bicarbonate solution (5%) and again with water and dried over anhydrous sodium sulphate. Evaporation of the solvent gave an oil which was chromatographed over silica gel (40 g). Each fraction of 20 ml was collected. Elution with light petroleum-ether (20:1) afforded the dinitrimine (CXCIII) which was recrystallized from methanol (0.5 g), m.p. 156°. $\nu_{max.}$ 1640 m(C=N), 1555-1565 s($\nu_{as}NO_2$) and 1315-1335 s($\nu_s NO_2$) cm^{-1} δ 2.9 m($C_5\alpha\underline{H}$), 0.93, 0.81, 0.7 and 0.63 (methyl protons).

Analysis Found : C, 66.5; H, 9.2; N, 11.3%

$C_{27}H_{44}N_4O_4$ requires : C, 66.4; H, 9.0; N, 11.5%.

Further elution with light petroleum-ether (15:1) gave the oxonitrimine (CXCIV) recrystallized from methanol (0.8 g),

m.p. 195°, $\nu_{max.}$ 1715 s(C_3-C=O), 1630 m(C=N), 1555 s($\nu_{as}NO_2$) and 1340 s(ν_sNO_2) cm^{-1}; δ 2.9 m($C_5\alpha$-$\underline{H}$), 2.7 m(C_7-$\underline{H}_2$), 2.3-2.5 m(C_2-$\underline{H}_2$ and C_4-$\underline{H}_2$), 0.91, 0.8, 0.73 and 0.68 (methyl protons).

Analysis Found : C, 72.8; H, 9.9; N, 6.5%

$C_{27}H_{44}N_2O_3$ requires : C, 73.0; H, 10.0; N, 6.3%

Elution with light petroleum-ether (10:1) furnished the ketone (CXCV) recrystallized from methanol (0.4 g), m.p. and m.m.p. 167°.

Hydrolysis of (CXCIII) and (CXCIV):3,6-Dioxo-5α-cholestane (CXCV)

The hydrolysis of the nitrimines (CXCIII) and (CXCIV) (0.5 g each) with dil hydrochloric acid (10 ml) furnished, after the evaporation of the solvent, a white solid which was filtered and recrystallized from methanol to give the dione (CXCV) (0.3 g), m.p. and m.m.p. 168° (lit.[118] m.p. 169°).

PART - TWO

Isomerization of 6-nitrimino-5α-cholestane (CLXIII):6-Nitro-aminocholest-5-ene (CXCVI)

6-Nitrimino-5α-cholestane (CLXIII) (1 g) was dissolved in methanol (100 ml) and potassium hydroxide pellets (1.2 g) were added to it. The mixture was stirred at room temperature for two hours. After the completion of the reaction, the contents were poured into acidified water. The organic material was extracted with ether and the ethereal solution was washed successively with water, sodium bicarbonate solution (5%) and again with water and dried over anhydrous sodium sulphate. Evaporation of the solvent gave an oily residue which was chromatographed over silica gel (20 g). Each fraction of 15 ml was collected. Elution with light petroleum-ether (25:1) afforded the nitroenamine (CXCVI) which was recrystallized from acetone (0.6 g), m.p. 130°. $\nu_{max.}$ 3320 m(N-H), 1620 w(C=C), 1535 s($\nu_{as}NO_2$) and 1320 s($\nu_{s}NO_2$) cm^{-1}; δ 8.5 br(N-H), 0.9, 0.83, 0.7 and 0.63 (methyl protons).

Analysis Found : C, 75.3; H, 10.5; N, 6.6%

$C_{27}H_{46}N_2O_2$ requires : C, 75.4; H, 10.7; N, 6.5%.

Acetylation of nitroenamine (CXCVI):O-Acetyl-6-aci-nitroamino-cholest-5-ene (CC-a)

6-Nitroaminocholest-5-ene (CXCVI) (0.2 g), acetic anhydride (0.5 ml) and pyridine (1 ml) were allowed to react at room temperature, under anhydrous conditions, for thirty minutes. The contents were poured into acidified cold water and extracted with ether. Usual work up and column chromatography over silica gel gave (CC-a) as a non-crystallizable oil (0.12 g); $\nu_{max.}$ 1738 s(O-$\overset{O}{\overset{\|}{C}}$-$CH_3$), 1600 w(C=C), 1570 w(-N=N→O), 1245 s and 1030 m(acetate) cm^{-1}; δ 2.06 s(CH_3-$\overset{O}{\overset{\|}{C}}$-O), 1.1, 0.93, 0.81 and 0.7 (methyl protons).

Analysis Found : C, 73.5; H, 10.3; N, 6.2%

$C_{29}H_{48}N_2O_3$ requires : C, 73.7; H, 10.2; N, 6.0%

Reduction of 6-nitrimino-5α-cholestane (CLXIII): 6β-Nitroamino-5α-cholestane (CXCVIII)

To a solution of 6-nitrimino-5α-cholestane (CLXIII) (1 g) in absolute ethanol (100 ml), sodium borohydride (1 g) was added and the mixture was stirred at ambient temperature for one and a half hour. The reaction mixture was then poured in water and extracted with ether. The ethereal solution was washed several times with water and dried over anhydrous sodium sulphate. Evaporation of the solvent gave an oily residue which was purified by column chromatography over silica gel (20 g). Each

fraction of 15 ml was collected. Elution with light petroleum-ether (30:1) gave 6β-nitroamino-5α-cholestane (CXCVIII) as a non-crystallizable oil (0.7 g); $\nu_{max.}$ 3300 m(N-H), 1535 s($\nu_{as}NO_2$) and 1330 s($\nu_{s}NO_2$) cm^{-1}; δ 8.75 d(N<u>H</u>, J = 6 Hz), 4.21 m($C_6\alpha$-H, $W\frac{1}{2}$ = 8 Hz), 0.93, 0.81, 0.7 and 0.68 (methyl protons).

Analysis Found : C, 74.8; H, 11.0; N, 6.6%

$C_{27}H_{48}N_2O_2$ requires : C, 75.0; H, 11.1; N, 6.5%.

<u>Acetylation of Nitroamine (CXCIX):O-Acetyl-6β-aci-nitroamino-5α-cholestane (CXCIX-a)</u>

6β-Nitroamino-5α-cholestane (CXCVIII) (0.3 g), acetic anhydride (0.5 ml) and pyridine (1 ml) were allowed to stand at room temperature, under anhydrous conditions for thirty minutes. The reaction mixture was poured into acidified cold water and the organic matter was extracted with ether. The ethereal solution was washed with water, dried (Na_2SO_4) and evaporated to give an oily residue. The purification of the oil by column chromatography over silica gel (light petroleum-ether 40:1 as eluent) afforded the N-oxidoacetate (CXCIX-a) as a non-crystallizable oil (0.2 g); $\nu_{max.}$ 1740 s(O-C(=O)-CH_3), 1572 w(-N=N⟶O), 1240m and 1030 s(acetate) cm^{-1}; δ 4.3 m($C_6\alpha$-<u>H</u>, $W\frac{1}{2}$ = 8 Hz), 2.15 s($C\underline{H}_3COO$), 0.91, 0.83, 0.71 and 0.68 (methyl protons).

Analysis Found : C, 73.2; H, 10.6; N, 5.7%

$C_{29}H_{50}N_2O_3$ requires : C, 73.56; H, 10.5; N, 5.9%.

Thermolysis of 6-nitrimino-5α-cholestane (CLXIII): Cholest-5-ene (CCI), 6-oxo-5α-cholestane (CLXIV), 6-oximino-5α-cholestane (CLXII) and 6-oxo-7α-hydroxy-5α-cholestane (CCII)

6-Nitrimino-5α-cholestane (CLXIII) (2 g) was dissolved in xylene (15 ml) and the mixture was refluxed for five hours. The excess of the solvent was then removed in vacuo and the brown coloured oil thus obtained was chromatographed over silica gel (40 g). Elution with light petroleum furnished cholest-5-ene (CCI), recrystallized from acetone (0.3 g), m.p. and m.m.p. 95°.

Further elution with light petroleum-ether (30:1) afforded the ketone (CLXIV) which was recrystallized from methanol (0.4 g) m.p. and m.m.p. 98°.

Continued elution with light petroleum-ether (20:1) gave the oxime (CLXII), recrystallized from methanol (0.3 g), m.p. and m.m.p. 200°.

Elution with light petroleum-ether (15:1) afforded (CCII) which was recrystallized from methanol (0.5 g), m.p. 185° ν max. 3360-3400 m(O-H), 1710 s(C_6-C=O)cm^{-1}; 3.7(C_7 β-H, $W\frac{1}{2}$ = 6 Hz), 0.93, 0.73 and 0.68 (methyl protons).

Analysis Found : C, 80.5; H, 11.5%

$C_{27}H_{46}O_2$ requires : C, 80.6; H, 11.4%.

Isomerization of 6-nitrimino-5α-cholestan-3β-yl chloride (CLXVIII):6-Nitroaminocholest-5-en-3βyl chloride (CCIII):

6-Nitrimino-5α-cholestan-3β-yl chloride (CLXVIII) (1 g) was dissolved in methanol (100 ml) and KOH pellets (1.2 g) were added to it. The reaction mixture was stirred at room temperature for two hours, poured into acidified cold water and extracted with ether. The ethereal solution was washed successively with water, sodium bicarbonate solution (5%) and again with water. Evaporation of the solvent gave an oil which on column chromatography over silica gel (20 g) (light petroleum-ether 20:1 as eluent) afforded the nitroenamine (CCIII) recrystallized from methanol (0.7 g), m.p. 165°. $\nu_{max.}$ 3480 m(N-H), 1620 w(C=C), 1570 s($\nu_{as}NO_2$), 1310 s($\nu_s NO_2$) and 750 m(C-Cl) cm^{-1}; δ 8.5 br(N<u>H</u>); 3.65 m($C_3\alpha$-<u>H</u>, $W\frac{1}{2}$ = 14 Hz), 0.9, 0.81 and 0.71 (methyl protons).

Analysis Found : C, 69.6; H, 9.6; N, 6.1%

$C_{27}H_{45}N_2O_2Cl$ requires : C, 69.8; H, 9.7; N, 6.0%.

Acetylation of nitroenamine (CCIII):O-Acetyl-6-<u>aci</u>-nitroamino-cholest-5-en-3β-yl chloride (CCIV)

6-Nitroaminocholest-5-en-3β-yl chloride (CCIII) (0.2 g), acetic anhydride (0.5 ml) and pyridine (1 ml) were allowed to react at room temperature for thirty minutes. The contents were poured into cold water and the organic matter was extracted

with ether. The ether layer was worked up as usual and dried over anhydrous sodium sulphate. Evaporation of the solvent gave an oily residue which was chromatographed over silica gel. Elution with light petroleum-ether (15:1) gave the N-oxidoacetate (CCIV) as a non-crystallizable oil (0.15 g), $\nu_{max.}$ 1740 s(CH_3-C(=O)-O), 1610 w(C=C), 1570 w(-N=N⟶O), 1240s, 1030 m(acetate) and 735 m(C-Cl) cm^{-1}; δ 3.8 m($C_3\alpha$-H, $W\frac{1}{2}$ = 17 Hz), 2.12 s(CH_3COO), 1.1, 0.91, 0.83 and 0.7 (methyl protons).

Analysis Found : C, 74.0; H, 9.7; N, 5.8%

$C_{29}H_{47}N_2O_3Cl$ requires : C, 73.9; H, 9.9; N, 5.9%.

Reduction of 6-nitrimino-5α-cholestan-3β-yl chloride (CLXVIII): 6β-Nitroamino-5α-cholestan-3β-yl chloride (CCV)

6-Nitrimino-5α-cholestan-3β-yl chloride (CLXVIII) (1 g) was dissolved in absolute ethanol (100 ml) and sodium borohydride (1 g) was added to it. The mixture was stirred at room temperature for two hours, poured into cold water and extracted with ether. The ethereal solution was washed several times with water and dried over anhydrous sodium sulphate. Evaporation of the solvent gave (CCV) as a non-crystallizable oil (0.7 g), $\nu_{max.}$ 3485 m(NH), 1560 s($\nu_{as}NO_2$), 1310 s(ν_sNO_2) and 740 m(C-Cl) cm^{-1}; δ 8.8 d(NH, J = 9 Hz), 4.2 m($C_6\alpha$-H, $W\frac{1}{2}$ = 6 Hz), 3.7 m($C_3\alpha$-H, $W\frac{1}{2}$ = 14 Hz), 0.93, 0.8, 0.75 and 0.6 (methyl protons).

Analysis Found : C, 69.6; H, 10.3; N, 5.8%

$C_{27}H_{47}N_2O_2Cl$ requires : C, 69.5; H, 10.1; N, 6.0%.

Acetylation of Nitroamine (CCV):O-Acetyl-6β-aci-nitroamino-5α-cholestan-3β-yl chloride (CCVI)

The nitroamine (CCV) (0.2 g) was dissolved in acetic anhydride (0.5 ml) and pyridine (1 ml) and allowed to stand at room temperature for thirty minutes. The solution was poured onto crushed ice and extracted with ether. Usual work of the ethereal solution followed by the evaporation of the solvent gave O-acetyl-6β-aci-nitroamino-5α-cholestan-3β-yl chloride (CCVI) as a noncrystallizable oil (0.12 g), $\nu_{max.}$ 1735 s(CH_3-C(=O)-O), 1570 w(-N=N⟶O), 1240s, 1030 m(acetate) and 750 m(C-Cl) cm^{-1}; δ 4.4 m($C_6\alpha$-H, $W_{\frac{1}{2}}$ = 7 Hz), 3.7 m($C_3\alpha$-H, $W_{\frac{1}{2}}$ = 16 Hz), 2.1 s(CH_3-COO), 0.93, 0.81, 0.7 and 0.63 (methyl protons).

Analysis Found : C, 73.5; H, 10.4; N, 6.0%

$C_{29}H_{49}N_2O_3Cl$ requires : C, 73.6; H, 10.3; N, 5.9%

Isomerization of 6-nitrimino-5α-cholestan-3β-yl acetate (LIV): 6-Nitroaminocholest-5-en-3β-ol (CCVII)

6-Nitrimino-5α-cholestan-3β-yl acetate (LIV) (1 g) was dissolved in methanol (100 ml) and potassium hydroxide pellets (1.2 g) were added to it. The mixture was stirred at ambient temperature for two hours. The contents were poured into water, acidified with dilute hydrochloric acid and extracted with ether. The ethereal solution was washed successively with water, sodium bicarbonate solution (5%) and again with

water and dried over anhydrous sodium sulphate. Evaporation of the solvent gave an oil which was crystallized from methanol to give (CCVII) (0.7 g), m.p. 158°. $\nu_{max.}$ 3460-3500 br (OH and NH), 1600 m(C=C), 1550 s($\nu_{as}NO_2$) and 1320 s($\nu_{s}NO_2$) cm^{-1}; δ 8.6 br(N<u>H</u>), 3.7 m($C_3\alpha$-<u>H</u>, $W\frac{1}{2}$ = 14 Hz), 0.93, 0.83, 0.7 and 0.68 (methyl protons).

Analysis Found : C, 72.6; H, 10.3; N, 6.3%

$C_{27}H_{46}N_2O_3$ requires : C, 72.4; H, 10.2; N, 6.4%.

<u>Reduction of 6-nitrimino-5α-cholestan-3β-yl acetate (LIV): 6β-Nitroamino-5α-cholestan-3β-ol (CCVIII)</u>

To a suspension of 6-nitrimino-5α-cholestan-3β-yl acetate (LIV) (0.5 g) in absolute ethanol (50 ml), was added sodium borohydride (0.5 g) and the mixture was stirred at room temperature for two hours. The reaction mixture was then poured into water and extracted with ether. The ethereal solution was washed several times with water and dried over anhydrous sodium sulphate. Evaporation of the solvent and crystallization from methanol furnished (CCVIII) (0.3 g), m.p. 192°. $\nu_{max.}$ 3400-3520 br(NH and OH), 1550 s, 1320 s(NO_2) and 1030 m(C-O) cm^{-1}; δ 8.9 d(N<u>H</u>, J = 7 Hz), 4.15 m($C_6\alpha$-<u>H</u>, $W\frac{1}{2}$ = 6 Hz), 3.75 m($C_3\alpha$-<u>H</u>, $W\frac{1}{2}$ = 18 Hz), 0.93, 0.81, 0.7 and 0.63 (methyl protons).

Analysis Found : C, 72.3; H, 10.7; N, 6.2%

$C_{27}H_{48}N_2O_3$ requires : C, 72.1; H, 10.5; N, 6.4%.

Acetylation of Nitroamine (CCVIII):O-Acetyl-6β-aci-nitroamino-5α-cholestan-3β-ol (CCIX)

A mixture of 6β-nitroamino-5α-cholestan-3β-ol (CCVIII) (0.2 g), acetic anhydride (0.5 ml) and pyridine (1 ml) was allowed to stand at room temperature for thirty minutes. The reaction mixture was then poured on to crushed ice and extracted with ether. The ethereal solution was washed several times with water and dried over anhydrous sodium sulphate. Evaporation of the solvent gave (CCIX) as an oil which failed to crystallize in any solvent (0.15 g); $\nu_{max.}$ 3420 m(OH), 1735 s($-O-\overset{O}{\overset{\|}{C}}-CH_3$), 1565 w($-N=N\longrightarrow O$), 1240 s(acetate) and 1030 m(C-O) cm^{-1}; δ 4.3 m($C_6\alpha$-H, $W\frac{1}{2}$ = 7 Hz), 3.7 m($C_3\alpha$-H, $W\frac{1}{2}$ = 1.6 Hz), 2.1 s(CH_3COO), 0.93, 0.8, 0.71 and 0.68 (methyl protons).

Analysis Found : C, 71.2; H, 10.0; N, 5.8%

$C_{29}H_{50}N_2O_4$ requires : C, 71.0; H, 10.2; N, 5.7%.

Thermolysis of 6-nitrimino-5α-cholestan-3β-yl acetate (LIV): Cholest-5-en-3β-yl acetate (CCX), 6-oxo-5β-nitrocholestan-3β-yl acetate (CCXI), 6-oxo-5α-cholestan-3β-yl acetate (CLXXI), 6-oximino-5α-cholestan-3β-yl acetate (CLXX) and 6-oxo-7α-hydroxy-5α-cholestan-3β-yl acetate (CCXIII)

6-Nitrimino-5α-cholestan-3β-yl acetate (LIV) (2 g) was dissolved in xylene (15 ml) and the mixture was heated under reflux for five hours. The excess of the solvent was removed

under reduced pressure and the oily residue thus obtained was chromatographed over silica gel (40 g). Each fraction of 20 ml was collected. Elution with light petroleum-ether (40:1) gave cholest-5-en-3β-yl acetate (CCX), recrystallized from acetone (0.4 g) m.p. and m.m.p. 115°.

Continued elution with the same solvent system afforded (CCXI) recrystallized from methanol (0.3 g), m.p. 75°, $\nu_{max.}$ 1730 s(CH_3COO), 1700 s(C_6-C=O), 1580 s(ν_{as} NO_2), 1370 s ($\nu_s NO_2$), 1240s and 1040 m(acetate) cm^{-1}; δ 5.05 m($C_3\alpha$-H, $W\frac{1}{2}$ = 6 Hz), 2.1 s(CH_3COO), 1.1, 0.93, 0.8 and 0.73 (methyl protons). MS, M^+ 489, m/z 443 (M^+-NO_2), 442 (M^+-HNO_2) and 383 (M^+-NO_2+AcOH).

Analysis Found : C, 71.0; H, 9.7; N, 3.0%

$C_{29}H_{47}NO_5$ requires : C, 71.1; H, 9.6; N, 2.9%.

Further elution with light petroleum-ether (30:1) furnished the ketone (CLXXI), recrystallized from methanol (0.5 g), m.p. and m.m.p. 127°.

Elution with light petroleum-ether (20:1) gave 6-oximino-5α-cholestan-3β-yl acetate (CLXX), recrystallized from methanol (0.2 g), m.p. and m.m.p. 200°.

Further elution with light petroleum-ether (10:1) afforded 6-oxo-7α-hydroxy-5α-cholestan-3β-yl acetate (CCXIII), recrys-

tallized from methanol (0.4 g), m.p. 235°. $\nu_{max.}$ 3430 m(OH), 1725 s(CH_3-C(=O)-O), 1701 s(C_6-C=O), 1240 m(acetate) and 1040 m(C-O) cm^{-1}; δ 4.8 m($C_3\alpha$-H, $W\frac{1}{2}$ = 14 Hz), 3.75 m($C_7\beta$-H, $W\frac{1}{2}$ = 5 Hz), 2.05 (CH_3COO), 0.93, 0.81, 0.7 and 0.63 (methyl protons); MS, M^+ 460, m/z 442(M^+-H_2O), 400 (M^+-AcOH), 382 (400-H_2O) and 372 (400-CO).

Analysis Found : C, 75.5; H, 10.5%

$C_{29}H_{48}O_4$ requires : C, 75.6; H, 10.4%.

Reduction of 7-nitriminocholest-5-en-3β-yl chloride (CLXXXVII): 7β-Nitroaminocholest-5-en-3β-yl chloride (CCXV)

To a stirred solution of the nitrimine (CLXXXVII) (1 g) in absolute ethanol (100 ml), was added sodium borohydride (1.2 g) and the reaction mixture was stirred at room temperature for two hours. It was diluted with an excess of water and the organic matter was extracted with ether. The ethereal solution was washed several times with water and dried (Na_2SO_4). Evaporation of the solvent gave (CCXV), recrystallized from methanol (0.7 g), m.p. 137°; $\nu_{max.}$ 3420 m(NH), 1620 m(C=C), 1550 s($\nu_{as}NO_2$), 1330 s(ν_sNO_2) and 750 m(C-Cl) cm^{-1}, δ 8.4 br(NH), 5.26 s(C_6-vinylic H), 4.3 m($C_7\alpha$-H, $W\frac{1}{2}$ = 8 Hz), 3.7 m($C_3\alpha$-H, $W\frac{1}{2}$ = 16 Hz), 1.1, 0.91, 0.83 and 0.7 (methyl protons).

Analysis Found : C, 69.7; H, 9.8; N, 6.1%

$C_{27}H_{45}N_2O_2Cl$ requires : C, 69.8; H, 9.7; N, 6.0%.

Acetylation of Nitroamine (CCXV):O-Acetyl-7β-aci-nitroaminocholest-5-en-3β-yl chloride (CCXVI)

A mixture of the nitroamine (CCXV) (0.3 g), acetic anhydride (0.5 ml) and pyridine (1 ml) was allowed to stand at room temperature for thirty minutes. The contents were poured onto crushed ice and the organic matter was extracted with ether. The ethereal layer was washed several times with water and dried over anhydrous sodium sulphate. Evaporation of the solvent gave (CCXVI) as a non-crystallizable oil (0.2 g), $\nu_{max.}$ 1730 s(CH_3-$\overset{O}{\overset{\|}{C}}$-O), 1610 w(C=C), 1565 w(-N=$\overset{|}{N}$⟶O), 1240 s, 1030 m(acetate) and 750 m(C-Cl) cm^{-1}; δ 5.6 d(C_6-vinylic H , J=6 Hz), 4.8 m($C_7\alpha$-H, $W\frac{1}{2}$ = 8 Hz), 3.75 m($C_3\alpha$-H, $W\frac{1}{2}$ = 17 Hz), 1.97 s(CH_3COO), 1.1 0.9, 0.8 and 0.71 (methyl protons).

Analysis Found : C, 68.8; H, 9.1; N, 5.6%

$C_{29}H_{47}N_2O_3Cl$ requires : C, 68.8; H, 9.3; N, 5.5%.

Thermolysis of 7-nitriminocholest-5-en-3β-yl chloride (CLXXXVII): 7-Oxocholesta-3,5-diene (CLXXXIX)

7-Nitriminocholest-5-en-3β-yl chloride (CLXXXVII) (1 g) in xylene (10 ml) was heated under reflux for five hours. Xylene was removed under reduced pressure and the oily residue thus obtained was chromatographed over silica gel (20 g). Each fraction of 20 ml was collected. Elution with light petroleum-ether (30:1) gave 7-oxo-cholesta-3,5-diene (CLXXXIX), recrystallized from methanol (0.6 g), m.p. and m.m.p. 112°.

PART - THREE

Oxymercuration of cholest-5-ene (CCI)

Cholest-5-ene (CCI) (4 g) was dissolved in THF (25 ml) and acetic acid (100 ml) was added to it. The solution was warmed and mercuric acetate (4 g) was added in portions with shaking. The mixture was heated under reflux for five hours. The reaction mixture was poured in cold water and extracted with dichloromethane. The organic layer was washed successively with water, sodium bicarbonate solution (5%) and again with water and dried over anhydrous sodium sulphate. Evaporation of dichloromethane under reduced pressure furnished the organomercury acetate adduct as a gum. No attempt was made to purify the adduct and it was as such subjected to demercuration reaction.

Dermercuration of the adduct with $NaBH_4$-NaOH: 5α-Cholestan-6β-ol (CCXXXIV) and cholest-4-en-6β-ol (CCXL)

The organomercury acetate adduct (2 g) was dissolved in THF (25 ml) and to this was added a solution of 2N sodium hydroxide (50 ml). The mixture was treated with sodium borohydride (2 g) dissolved in 2N sodium hydroxide solution (25 ml) and stirred at ambient temperature for five hours. After the completion of the reaction, the mixture was poured

into water, acidified with dilute hydrochloric acid and extracted with ether. The ethereal solution was washed successively with water, sodium bicarbonate solution (5%) and again with water and dried over anhydrous sodium sulphate. Evaporation of the solvent gave an oily residue which was chromatographed over silica gel (40 g). Each fraction of 20 ml was collected. Elution with light petroleum-ether (15:1) furnished the alcohol (CCXXXIV), recrystallized from methanol (0.7 g), m.p. 80° (lit.[145] m.p. 80-82°). $\nu_{max.}$ 3410 m(O-H) and 1030 m(C-O) cm^{-1}; δ 3.7 m($C_6\alpha$-$\underline{H}$, $W\frac{1}{2}$ = 6 Hz), 0.9, 0.81, 0.73 and 0.68 (methyl protons).

Analysis Found : C, 83.7; H, 12.1%
$C_{27}H_{48}O$ requires : C, 83.5; H, 12.4%.

Further elution with light petroleum-ether (10:1) gave the allylic alcohol (CCXL), recrystallized from acetone (0.8 g), m.p. 140°. $\nu_{max.}$ 3500 m(O-H), 3030 w(C=C-H), 1650 m(C=C) and 1030 m(C-O) cm^{-1}; δ 5.61 m(C_4-vinylic $\underline{H}$), 3.9 m($C_6\alpha$-$\underline{H}$, $W\frac{1}{2}$ = 6 Hz), 0.96, 0.9, 0.83 and 0.7 (methyl protons).

Analysis Found : C, 83.8; H, 12.0%
$C_{27}H_{46}O$ requires : C, 83.9; H, 11.9%.

Jones' Oxidation of (CCXXXIV):6-oxo-5α-cholestane (CLXIV)

The alcohol (CCXXXIV) (0.2 g) was suspended in acetone (10 ml) and Jones' reagent (10 drops) was added to it with

stirring. The temperature of the reaction mixture during the oxidation was maintained between 0-5°C. After completion of the reaction the mixture was diluted with ice cold water and the organic matter was extracted with ether. The ethereal solution was washed with water, sodium bicarbonate solution (5%) and again with water and dried over anhydrous sodium sulphate. Evaporation of ether gave an oily residue which was crystallized from methanol to give 6-oxo-5α-cholestane (CLXIV) (150 mg), m.p. and m.m.p. 97° (lit.[100] m.p. 96-98°).

Acetylation of (CCXXXIV):5α-Cholestan-6β-yl acetate (CCXXXVIII)

Amixture of 5α-cholestan-6β-ol (CCXXXIV) (0.2 g), acetic anhydride (0.2 ml) and pyridine (0.5 ml) was heated on a water bath for two hours. The contents were poured into crushed ice and the organic matter was extracted with ether. The ethereal solution was washed with water and dried over anhydrous sodium sulphate. Evaporation of the solvent gave 5α-cholestan-6β-ylacetate (CCXXXVIII) as a non-crystallizable oil (0.15 g). $\nu_{max.}$ 1735 s($CH_3\overset{O}{\overset{\|}{C}}$-O), 1240 m(acetate) and 1030 m(C-O) cm^{-1}; δ4.6 m($C_6\alpha$-H, $W\frac{1}{2}$ = 6 Hz), 2.1 s(CH_3COO), 0.97, 0.91, 0.81 and 0.67 (methyl protons).

Analysis Found : C, 80.7; H, 11.5%

$C_{29}H_{50}O_2$ requires : C, 80.9; H, 11.6%.

Acetylation of (CCXL):Cholest-4-en-6β-yl acetate (CCXLII)

A mixture of (CCXL) (0.5 g), acetic anhydride (0.5 ml) and pyridine (1 ml) was heated on a steam bath for two hours. The reaction mixture was poured onto crushed ice and the organic matter was extracted with ether. The ethereal solution was washed with water and dried (Na_2SO_4). Evaporation of the solvent gave (CCXLII)as an oil (0.4 g), $\nu_{max.}$ 3030 w(C=C-H), 1730 s($CH_3\overset{O}{\overset{\|}{C}}$-O), 1240 m(acetate)and 1030 m(C-O) cm^{-1}; δ 5.7 m(C_4-vinylic H), 4.8 m($C_6\underline{H}$, $W\frac{1}{2}$ = 6 Hz), 2.01 s($C\underline{H}_3COO$), 0.98, 0.9, 0.8 and 0.7 (methyl protons).

Analysis Found : C, 81.5; H, 11.1%

$C_{29}H_{48}O_2$ requires : C, 81.3; H, 11.2%.

Demercuration of organomercury acetate adduct with $NaBH_4$-Ethylene Glycol:6-Oxocholest-4-ene (CCXLIII), 6-oxocholest-4-en-3β,7β-yl diacetate (CCXLIV), 7-oxocholest-5-en-4α-yl acetate (CCXLV), 6-oxocholest-4-en-7α-yl acetate (CCXLVI) and 7-oxocholest-4-en-6β-ol-3β-yl acetate (CCXLVII)

The organomercury acetate adduct (2 g) of cholest-5-ene was dissolved in THF (25 ml) and ethylene glycol (25 ml) was added to it. The mixture was treated with sodium borohydride (2 g) and the contents were stirred at room temperature for six hours. The reaction mixture was then poured into water and the organic matter was extracted with ether. The ethereal

solution was washed several times with water and dried over anhydours sodium sulphate. Evaporation of the solvent gave an oil which was chromatographed over silica gel (40 g). Each fraction of 20 ml was collected. Elution with light petroleum-ether (20:1) furnished 6-oxocholest-4-ene (CCXLIII), recrystallized from methanol (0.3 g), m.p. 105° (lit.[146] m.p. 108-110°) $\nu_{max.}$ 1680 s(C=C-C=O) and 1620 s(C=C) cm^{-1}, δ 6.4 m(C_4-vinylic H) 0.96, 0.91, 0.83 and 0.7 (methyl protons).

Continued elution with light petroleum-ether (20:1) gave 6-oxocholest-4-en-3β, 7β-yl diacetate (CCXLIV) as a non-crystallizable oil (0.5 g), $\nu_{max.}$ 3060 w(C=C-H), 1740 br s(CH_3COO), 1680 s(C=C-C=O), 1635 m(C=C), 1240 br(acetate) and 1020 m(C-O) cm^{-1}, δ 5.56 m(C_4-vinylic H), 5.2 br s($C_7\alpha$-H), 5.1 m($C_3\alpha$-H, $W\frac{1}{2}$ = 16 Hz), 2.1 s(CH_3COO), 2.03 s(CH_3COO), 0.95, 0.81, 0.73 and 0.7 (methyl protons).

Analysis Found : C, 74.6; H, 9.8%

$C_{31}H_{48}O_5$ requires : C, 74.4; H, 9.6%.

Further elution with light petroleum-ether (15:1) afforded (CCXLV) as a non-crystallizable oil (0.3 g). $\nu_{max.}$ 3030 w(C=C-H), 1740 s(CH_3-C(=O)-O), 1670 s(C=C-C=O), 1610 m(C=C), 1240 m(acetate) and 1030 m(C-O) cm^{-1}; δ 6.03 s(C_6-vinylic H), 5.2 m($C_4\beta$-H, $W\frac{1}{2}$ = 9 Hz), 1.97 s(CH_3COO), 0.9, 0.83, 0.75 and 0.7 (methyl protons).

Analysis Found : C, 78.5; H, 10.2%

$C_{29}H_{46}O_3$ requires : C, 78.7; H, 10.4%.

Elution with light petroleum-ether (12:1) furnished 6-oxocholest-4-en-7α-yl acetate (CCXLVI) as an oil which failed to crystallize (0.4 g). $\nu_{max.}$ 3030 w(C=C-H), 1735 s(CH_3-$\overset{O}{\overset{\|}{C}}$-O), 1680 s(C=C-C=O), 1620 m(C=C), 1235 m(acetate) and 1030 m(C-O) cm^{-1}; δ 5.8 m(C_4-vinylic H), 5.35 br s(C_7β-H), 2.0 s(CH_3COO), 0.93, 0.83, 0.75 and 0.68 (methyl protons).

Analysis Found : C, 78.5; H, 10.5%

$C_{29}H_{46}O_3$ requires : C, 78.7; H, 10.4%.

The elution of the column with light petroleum-ether (5:1) gave 7-oxocholest-4-en-6β-ol-3β-yl acetate (CCXLVII) which failed to crystallize and was isolated as an oil (0.25 g), $\nu_{max.}$ 3420 m(O-H), 3030 w(C=C-H), 1735 s(CH_3-$\overset{O}{\overset{\|}{C}}$-O), 1715 s(C=O), 1610 m(C=C), 1240 m(acetate) and 1030 m(C-O) cm^{-1}; δ 5.56 br s(C_4-vinylic H), 5.01 m(C_3α-H, $W\frac{1}{2}$ = 14 Hz), 4.15 m(C_6α-H, $W\frac{1}{2}$ = 5 Hz), 1.95 s(CH_3COO), 1.1, 0.89, 0.81 and 0.71 (methyl protons).

Analysis Found : C, 75.8; H, 10.1%

$C_{29}H_{46}O_4$ requires : C, 76.0; H, 10.0%.

Oxymercuration of cholest-5-en-3β-yl chloride (CCXXXII)

Cholest-5-en-3β-yl chloride (CCXXXII) (4 g) was dissolved in THF (25 ml) and acetic acid (100 ml) was added to it. The

solution was warmed and mercuric acetate (8 g) was added in portions with shaking. The reaction mixture was heated under reflux for six hours and poured into cold water. The organic matter was extracted with dichloromethane washed successively with water, sodium bicarbonate solution (5%) and again with water and dried over anhydrous sodium sulphate. Evaporation of the solvent under reduced pressure furnished the organomercurial adduct as a gum. The adduct was then subjected to demercuration reaction under different conditions.

Demercuration of the adduct with $NaBH_4$-NaOH:Cholest-5-en-3β-ol (CCXXXVII) and 5α-cholestane-3β, 6β-diol (CCXLVIII)

The organomercury acetate adduct (2 g) was dissolved in THF (25 ml) and a solution of 2N sodium hydroxide (50 ml) was added to it. The mixture was treated with sodium borohydride (2 g) dissolved in 2N sodium hydroxide solution (25 ml) and the suspension was stirred at room temperature for five hours. The reaction mixture was poured into water, acidified with dilute hydrochloric acid and extracted with ether. The ethereal solution was washed successively with water, sodium bicarbonate solution (5%) and again with water and dried over anhydrous sodium sulphate. Evaporation of the solvent gave an oil which was chromatographed over silica gel (40 g). Each fraction of 20 ml was collected. Elution with light petroleum ether (10:1) furnished cholest-5-en-3β-ol (CCXXXVII), recrystallized from

ethanol (1.2 g), m.p. and m.m.p. 150° (lit.[147] m.p. 149-150°).

Further elution with light petroleum-ether (8:1) furnished (CCXLVIII), as a non-crystallizable oil (0.5 g). $\nu_{max.}$ 3460-3380 m(OH); δ 3.7 br m($C_3\alpha$-H and $C_6\alpha$-H), 0.91, 0.83, 0.71 and 0.68 (methyl protons).

Analysis Found : C, 80.0; H, 11.7%

$C_{27}H_{48}O_2$ requires : C, 80.2; H, 11.9%.

Jones' Oxidation of (CCLXVIII)

The diol (CCLXVIII) (0.2 g) was suspended in acetone (10 ml) and was cooled in an ice bath. Jones' reagent (few drops) was added to the suspension with continuous stirring. The reaction mixture was stirred for about thirty minutes, poured onto crushed ice and extracted with ether. The ethereal solution was washed with water and dried (Na_2SO_4). Evaporation of the solvent gave an oil which was crystallized from methanol to give 3,6-dioxo-5α-cholestane (CXCV) (0.15 g), m.p. and m.m.p. 165° (lit.[118] m.p. 169°).

Demercuration of the adduct with $NaBH_4$-Ethylene Glycol:Cholest-5-en-3β-yl acetate (CCX) and 5α-cholestane-3β,6β——yl diacetate (CCXLIX)

The organomercurial adduct (2 g) of cholest-5-en-3β-yl chloride was dissolved in THF (25 ml) and ethylene glycol (25 ml)

was added to it. The mixture was treated with sodium borohydride (2 g) and the contents were stirred at room temperature for four hours. The reaction mixture was then poured into water and the organic matter was extracted with ether. The ethereal solution was washed several times with water and dried over anhydrous sodium sulphate. Evaporation of the solvent gave an oil which was chromatographed over silica gel (40 g). Each fraction of 20 ml was collected. Elution with light petroleum-ether (30:1) gave cholest-5-en-3β-yl acetate (CCX), recrystallized from acetone (1.0 g), m.p. and m.m.p. 115°.

Further elution with light petroleum-ether (20:1) furnished 5α-cholestane-3β-6β-diol diacetate (CCXLIX) as a non-crystallizable oil (0.6 g), $\nu_{max.}$ 1730-1740 s(O-$\overset{O}{\overset{\|}{C}}$-$CH_3$), 1240 s(acetate) and 1030 (C-O) cm^{-1}; δ 4.6-4.7 br m($C_3\alpha$-H and $C_6\alpha$-H), 2.1 s(CH_3COO), 2.01 s(CH_3COO), 0.93, 0.8, 0.73 and 0.68 (methyl protons).

Analysis Found : C, 76.4; H, 10.5%

$C_{31}H_{52}O_4$ requires : C, 76.2; H, 10.6%.

Hydrolysis of (CCXLIX):5α-Cholestane-3β,6β-diol (CCXLVIII)

The diacetate (CCXLIX) (0.2 g) was dissolved in methanol (10 ml) and was treated with potassium hydroxide (0.5 g). The reaction mixture was stirred at room temperature for two hours. It was then diluted with water, acidified and extracted with ether. The ethereal solution was washed successively with

water, sodium bicarbonate solution (5%) and again with water and dried (Na_2SO_4). Evaporation of the solvent gave an oil (0.15 g) which was found to be identical in all respects with the diol (CCXLVIII).

The Jones' oxidation of (CCXLVIII), as described earlier, furnished 3,6-dioxo-5α-cholestane (CXCV) m.p. and m.m.p. 165°.

Reduction of 6-nitrocholest-5-ene (CCL) with zinc-acetic acid without added water:6-Oxo-5α-cholestan (CLXIV), 6-oximino-5α-cholestane (CLXII) and N-acetyl-N-acetyloxy-6-aminocholest-5-ene (CCLI)

A mixture of acetic acid (40 ml) and acetic anhydride (20 ml) was heated under reflux for one hour under anhydrous conditions. 6-Nitrocholest-5-ene (CCL) (2 g) was dissolved in the above mixture and zinc dust (4 g) was gradually added with continuous stirring over a period of thirty minutes, maintaining the anhydrous conditions throughout. The reaction mixture was then heated under reflux for four hours, poured onto crushed ice and immediately worked up with ether. The ethereal solution was washed successively with water, sodium bicarbonate solution (5%) and again with water and dried over anhydrous sodium sulphate. Evaporation of the solvent gave an oily residue which was chromatographed over silica gel (40 g). Elution with light petroleum-ether (20:1) furnished 6-oxo-5α-cholestane

(CLXIV), recrystallized from ethanol (0.2 g), mp. and m.m.p. 97°.

Further elution with light petroleum ether (15:1) gave the oxime (CLXII), recrystallized from methanol (0.3 g), m.p. and m.m.p. 200°.

Elution of the column with light petroleum-ether (8:1) afforded (CCLI) as a non-crystallizable oil (1.1 g). $\nu_{max.}$ 1710 s(CH_3-$\underset{\underset{O}{\|}}{C}$-O-), 1670 s($CH_3$-$\underset{\underset{O}{\|}}{C}$-N), 1230-1250 s(acetate) cm^{-1}; δ 2.3 s(-$\underset{\underset{O}{\|}}{C}$-$CH_3$), 2.1 s(-$\underset{\underset{O}{\|}}{C}$-$CH_3$), 1.1, 0.91, 0.81 and 0.7 (methyl protons).

Analysis Found : C, 76,5; H, 10.6; N, 2.8%

$C_{31}H_{51}NO_3$ requires : C, 76.7; H, 10.5; N, 2.9%.

Reduction of 6-nitrocholest-5-en-3β-yl chloride (CCLV):6-Oxo-5α-cholestan-3β-yl chloride (CLXIX), 6-oximino-5α-cholestan-3β-yl chloride (CLXVII) and N-acetyl-6-aminocholest-5-en-3β-yl chloride (CCLVI)

A mixture of glacial acetic acid (40 ml) and acetic anhydride was refluxed for one hor under anhydrous conditions. 6-Nitrocholest-5-en-3β-yl chloride (CCLV) (2 g) was dissolved in the above mixture and zinc dust (4 g) was added gradually with continuous stirring over a period of thirty minutes. The reaction mixture was then heated under reflux for four

hours, poured onto crushed ice and immediately worked up with ether. The ethereal solution was washed successively with water, sodium bicarbonate solution (5%) and again with water and dried over anhydrous sodium sulphate. Evaporation of the solvent gave an oil which was chromatographed over silica gel (40 g). Each fraction of 20 ml was collected. Elution with light petroleum-ether (30:1) afforded the ketone (CLXIX), recrystallized from methanol (0.25 g), m.p. and m.m.p. 128°.

Further elution with light petroleum-ether (20:1) gave the oxime (CLXVII), recrystallized from methanol (0.4 g), m.p. and m.m.p. 175°.

Elution with light petroleum-ether (10:1) furnished (CCLVI) (0.8 g), m.p. 103°. $\nu_{max.}$ 3420 m(NH), 1660 s(N-$\overset{O}{\overset{\|}{C}}$-$CH_3$), 1620 w((C=C) and 750 m(C-Cl) cm^{-1}; δ 8.6 br(NH), 3.7 m($C_3\alpha$-H, $W\frac{1}{2}$ = 16 Hz), 2.01 (CH_3CON), 1.1, 0.93, 0.81 and 0.7 (methyl protons).

Analysis Found : C, 75.3; H, 10.5; N, 3.1%

$C_{29}H_{48}NOCl$ requires : C, 75.5; H, 10.4; N, 3.0%.

Reduction of 6-nitrocholest-5-en-3β-yl acetate(CXLVIII):6-Oxo-5α-cholestan-3β-yl acetate (CLXXI), 6-oximino-5α-cholestan-3β-yl acetate (CLXX) and N-acetyl-6-aminocholest-5-en-3β-yl acetate (CCLVII)

6-Nitrocholest-5-en-3β-yl acetate (CXLVIII) (2 g) was dissolved in a mixture of acetic acid (40 ml) and acetic

anhydride (20 ml) by warming. Zinc dust (4 g) was gradually added over a period of thirty minutes with continuous stirring. The reaction mixture was then heated under reflux for four hours, poured onto crushed ice and immediately worked up with ether. The ethereal solution was washed successively with water, sodium bicarbonate solution (5%) and again with water and dried over anhydrous sodium sulphate. Evaporation of the solvent gave an oily residue which was chromatographed over silica gel (40 g). Each fraction of 25 ml was collected. Elution with light petroleum-ether (30:1) gave the ketone (CLXXI), recrystallized from methanol (0.3 g), m.p. and m.m.p. 127°.

Further elution with light petroleum-ether (20:1) furnished the oxime (CLXX), recrystallized from methanol (0.5 g), m.p. and m.m.p. 200°.

Elution with light petroleum-ether (5:1) afforded N-acetyl-6-aminocholest-5-en-3β-yl acetate (CCLVII), recrystallized from light petroleum (0.8 g), m.p. 165° $\nu_{max.}$ 3350-3300 m(NH), 1725 s(O-$\overset{O}{\overset{\|}{C}}$-$CH_3$), 1660 s(N-$\overset{O}{\overset{\|}{C}}$-$CH_3$), 1240 s(acetate) and 1030 m(C-O)cm^{-1}; δ 7.4 br(N$\underline{H}$CO), 4.5 m(C$_3\alpha$-$\underline{H}$, $W\frac{1}{2}$ = 14 Hz), 1.98 s($C\underline{H}_3$CO), 1.91 s($C\underline{H}_3$CO), 1.07, 0.91. 0.83 and 0.7 (methyl protons).

Analysis Found : C, 76.8; H, 10.4; N, 2.9%

$C_{31}H_{51}NO_3$ requires : C, 76.7; H, 10.5; N, 2.9%.

PART - FOUR

The mass spectra were measured on an AEI MS-9 and GC-MS JMS D300 mass spectrometers at 70 eV using a direct insertion technique at a source temperature of about 200°C.

The values (m/z) of the fragment ions from various nitro-olefins and nitrimines are tabulated below. The values in parentheses are the relative abundance (%) of the peaks with respect to the base peak taken as 100%.

6-Nitrocholest-5-ene (CCL)

$M^{+\cdot}$ 415 (68.9; $C_{27}H_{45}NO_2$), 400 (15.5), 399 (24.4), 398 (77.7), 397 (8.8), 385 (13.3), 383 (.5.5), 382 (8.8), 372 (17.7), 371 (22.2), 370 (44.4), 369 (68.9), 368 (40.0), 367 (11.1), 356 (8.8), 355 (11.1), 353 (8.8), 342 (4.4), 330 (4.4), 328 (4.4), 316 (4.4), 314 (4.4), 302 (4.4), 300 (4.4), 286 (17.7), 274 (6.6), 272 (11.1), 260 (6.6), 258 (13.3), 255 (13.3), 247 (15.5), 244 (17.7), 230 (13.3), 218 (15.5), 215 (15.5), 213 (8.8), 175 (17.7), 161 (31.1), 159 (26.6), 149 (20.0), 147 (28.8), 145 (22.2), 138 (17.7), 135 (24.4), 133 (20.0), 131 (15.5), 123 (22.2), 121 (33.3), 119 (22.2), 117 (11.1), 111 (31.1), 109 (40.0), 107 (37.7), 105 (35.5), 97 (26.6), 95 (88.9), 93 (55.5), 91 (37.7), 83 (44.4), 81 (68.9), 79 (40.0), 77 (17.7), 74 (17.7), 71 (48.9),

69 (66.6), 67 (48.9), 59 (53.3), 57 (88.9) and 55 (100).

6-Nitrocholest-5-en-3β-yl chloride (CCLV)

$M^{+\cdot}$ 449/451 (88.5/30.0; $C_{27}H_{44}NO_2Cl$), 434/436 (34.2/5.7), 432/434 (55.7/34.2), 419/421 (21.4/7.1), 416 (10.0), 414 (28.5), 413 (15.7), 403/405 (57.1/21.4), 398 (4.3), 396 (14.3), 383 (21.4), 370 (7.1), 368 (14.3), 356 (8.5), 355 (5.7), 336/338 (8.5/2.8), 329 (8.5), 320/322 (5.7/2.1), 308/310 (7.1/2.8), 278/280 (21.4/8.5), 209/211 (12.8/4.3), 195 (15.7), 193 (12.8), 183 (7.1), 181 (5.7), 172 (14.2), 161 (8.5), 159 (15.7), 157 (14.3), 147 (12.8), 145 (14.3), 143 (10.0), 135 (20.0), 133 (14.3), 131 (10.0), 123 (10.0), 121 (14.3), 119 (17.1), 109 (24.3), 107 (28.5), 105 (22.8), 97 (18.5), 95 (57.1), 91 (32.8), 83 (34.2), 81 (60.0), 79 (31.4), 77 (14.3), 71 (44.3), 69 (65.7), 67 (35.7), 57 (91.4), 55 (100).

6-Nitrocholest-5-en-3β-yl acetate (CXLVIII)

$M^{+\cdot}$ 473 ($C_{29}H_{47}NO_4$), 413 (23.4), 398 (11.1), 396 (20.0), 385 (17.7), 384 (40.0), 383 (48.9), 370 (22.2), 368 (35.5), 366 (13.3), 365 (8.8), 356 (20.0), 342 (6.6), 329 (24.4), 314 (6.6), 300 (6.6), 286 (4.4), 284 (4.4), 282 (4.4), 272 (4.4), 261 (4.4), 175 (13.3), 173 (13.3), 171 (6.6), 166 (11.1), 163 (8.8), 161 (11.1), 159 (22.2), 157 (17.7), 149 (17.7), 147 (20.0), 145 (24.4), 143 (17.7), 137 (13.3), 135 (35.5),

133 (22.2), 131 (15.5), 129 (11.1), 123 (22.2), 121 (33.3), 119 (31.1), 117 (17.7), 111 (15.5), 109 (42.2), 107 (62.2), 105 (35.5), 97 (28.8), 95 (86.6), 93 (44.4), 91 (42.2), 85 (13.3), 83 (42.2), 81 (91.1), 79 (40.0), 77 (17.7), 71 (51.1), 69 (88.9), 67 (44.4), 60 (28.8), 57 (100), 55 (95.5).

6-Nitrimino-5α-Cholestane (CLXIII)

$M^{+\cdot}$ 430 ($C_{27}H_{46}N_2O_2$), 384 (10.00), 371 (2.5), 370 (12.5), 369 (2.5), 368 (5.0), 340 (3.75), 330 (5.0), 298 (2.5), 288 (2.5), 272 (7.5), 244 (7.5), 230 (7.5), 176 (5.0), 162 (5.0), 161 (5.0), 160 (7.5), 159 (5.0), 158 (5.0), 151 (5.0), 150 (5.0), 149 (5.0), 135 (10.0), 133 (7.5), 123 (7.5), 122 (5.0), 121(5.0), 109 (10.0), 108 (7.5), 107 (15.0), 97 (22.5), 95 (32.5), 93 (17.5), 91 (10.0), 83 (22.5), 81 (32.5), 79 (17.5), 71 (20.0), 69 (25.0), 67 (25.0), 57 (50.0), 55 (67.5) and 43 (100.0).

6-Nitrimino-5α-Cholestan-3β-yl acetate (LIV)

$M^{+\cdot}$ 488 (4, $C_{29}H_{48}N_2O_4$), 472 (5.0), 471 (10.0), 470 (6.0), 459 (10.0), 458 (24.0), 442 (47.0), 440 (40.0), 429 (17.0), 428 (26.0), 426 (17.0), 412 (11.0), 410 (20.0), 390 (69.0), 382 (100.0), 372 (9.0), 370 (18.0), 369 (44.0), 368 (52.0), 366 (17.0), 356 (15.0), 355 (17.0), 353 (8.0), 342 (9.0), 340 (8.0), 331 (15.0), 330 (33.0), 319 (4.0), 318 (15.0), 316 (10.0), 302 (10.0), 290 (10.0), 288 (19.0).

271 (15.0), 270 (12.0), 262 (15.0), 244 (26.0), 239 (25.0), 228 (25.0), 211 (18.0), 200 (9.0), 185 (15.0), 181 (10.0), 174 (19.0), 163 (13.0), 161 (21.0), 160 (21.0), 159 (21.0), 157 (15.0), 149 (27.0), 148 (16.0), 147 (25.0), 146 (22.0), 136 (27.0), 135 (61.0), 133 (36.0), 131 (23.0), 123 (31.0), 121 (52.0), 119 (41.0), 111 (19.0), 110 (22.0), 109 (61.0), 107 (75.0), 105 (44.0), 97 (34.0), 95 (100.0), 93 (90.0), 91 (49.0), 83 (49.0), 81 (100.0), 80 (19.0), 79 (71.0), 71 (62.0), 69 (85.0), 67 (100.0), 57 (100.0) and 55 (100.0).

6-Nitrimino-3α,5-cyclo-5α-cholestane (CLXXIII)

$M^{+\cdot}$ 428 (7.5, $C_{27}H_{44}N_2O_2$), 399 (10.0), 398 (37.5), 383 (47.5), 382 (100.0), 371 (5.0), 370 (15.0), 369 (7.5), 368 (12.5), 356 (5.0), 355 (12.5), 354 (10.0), 174 (7.5), 161 (5.0), 160 (6.2), 159 (6.2), 158 (5.0), 157 (5.0), 148 (3.7), 147(5.0), 146 (5.0), 145 (5.0), 137 (7.5), 135 (17.5), 133 (7.5), 131(5.0), 121 (12.5), 120 (17.5), 118 (10.0), 109 (10.0), 107 (15.0), 105 (10.0), 95 (62.5), 93 (35.0), 91 (20.0), 83 (15.0), 81 (25.0), 79 (27.5), 77 (10.0), 71 (15.0), 69 (20.0), 67 (17.5), 57 (35.0), 55 (35.0) and 43 (90.0).

7-Nitriminocholest-5-ene (CLXXXIII)

$M^{+\cdot}$ 428($C_{27}H_{44}N_2O_2$), 398 (20.0), 383 (40.0), 382 (100.0), 380 (10.0), 370 (35.0), 368 (5.0), 366 (5.0), 300 (3.7), 274 (5.0), 270 (6.2), 268 (6.2), 212 (5.0), 202 (7.5), 188 (10.0),

176 (7.5), 174 (7.5), 163 (5.0), 162 (12.5), 134 (20.0), 121 (7.5), 109 (12.5), 107 (15.0), 97 (7.5), 95 (15.0), 93 (12.5), 91 (7.5), 85 (17.5), 83 (20.0), 81 (20.0), 77 (15.0), 71 (32.5), 69 (25.0), 67 (10.0), 57 (62.5), 55 (50.0) and 43 (65.0).

7-Nitriminocholest-5-en-3β-yl acetate (LV)

$M^{+\cdot}$ 486($C_{29}H_{46}N_2O_4$), 456 (7.5), 441 (25.0), 440 (25.0), 426 (5.0), 414 (5.0), 396 (10.0), 383 (7.5), 382 (37.5), 381 (42.5), 368 (35.0), 296 (5.0), 268 (7.5), 200 (7.5), 186 (12.5), 174 (20.0), 160 (15.0), 132 (20.0), 109 (7.5), 107 (10.0), 105 (12.5), 93 (17.5), 91 (12.5), 81 (20.0), 79 (10.0), 77(5.0), 71 (10.0), 69 (15.0), 67 (10.0), 60 (12.5), 57 (25.0), 55 (25.0), 45 (22.5) and 43 (100.0).

Syn-3-nitriminocholest-4-ene (CLXXVII)

$M^{+\cdot}$ 428($C_{27}H_{44}N_2O_2$), 413 (20.0), 412 (22.5), 399 (20.0), 398 (57.5), 397 (12.5), 396 (30.0), 386 (25.0), 383 (20.0), 382 (10.0), 368 (5.0), 367 (7.5), 366 (7.5), 327 (10.0), 315 (2.5), 300 (7.5), 271 (7.5), 260 (17.5), 258 (12.5), 244 (12.5), 229 (30.0), 201 (5.0), 175 (6.2), 173 (7.5), 161 (7.5), 159(7.5), 149 (17.5), 147 (22.5), 137 (10.0), 135 (20.0), 133 (17.5), 131 (10.0), 123 (20.0), 121 (22.5), 119 (20.0), 109 (22.5), 107 (27.5), 105 (25.0), 97 (12.5), 95 (37.5), 93 (30.0), 91(25.0),

83 (12.5), 81 (37.5), 79 (32.5), 77 (12.5), 71 (20.0), 69 (30.0), 67 (27.5), 57 (45.0), 55 (55.0) and 43 (100.0).

Anti-3-nitriminocholest-4-ene (CLXXVI)

$M^{+\cdot}$ 428($C_{27}H_{44}N_2O_2$), 413 (20.0), 412 (15.0), 399 (12.5), 398 (27.5), 396 (20.0), 386 (17.5), 383 (17.5), 382 (10.0), 369 (10.0), 366 (7.5), 327 (12.5), 315 (2.5), 300 (12.5), 288 (20.0), 286 (12.5), 271 (5.0), 260 (12.5), 244 (7.5), 229 (27.5), 201 (5.0), 187 (7.5), 175 (5.0), 173 (5.0), 161 (5.0), 159 (7.5), 149 (15.0), 147 (17.5), 135 (20.0), 133(15.0), 123 (25.0), 121 (22.5), 119(17.5), 111 (12.5), 109 (22.5), 107 (27.5), 105 (22.5), 95 (40.0), 93 (35.0), 91 (30.0), 83 (17.5), 81 (45.0), 79 (32.5), 71 (22.5), 69 (30.0), 67 (25.0), 57 (56.0), 55 (75.0) and 43 (100.0).

R E F E R E N C E S

1. V. Meyer, Ber., 6, 1492 (1873).

2. V. Meyer and Locher, Ber., 7, 788 (1874).

3. V. Meyer and Locher, Ber., 7, 1506 (1874).

4. W.A. Tilden and W.A. Shenstone, J. Chem. Soc., 554 (1877).

5. L. Claisen and O. Manasse, Ber., 22, 530 (1889).

6. D.T. Manning and H.A. Stansbury Jr., J. Am. Chem. Soc., 81, 4885 (1959).

7. C. Neuberg and E. Hofmann, Biochem. Z., 229, 443 (1930).

8. C. Neuberg and E. Hofmann, Biochem. Z., 239, 495 (1931).

9. S. Cusmano, Gazz. Chim. Ital., 68, 129 (1938).

10. D.H.R. Barton, J.M. Beaton, L.E. Geller and M.M. Pechet, J.Am. Chem. Soc., 83, 4076 (1961).

11. C.J. Thoman and I.M. Hunsberger, J. Org. Chem., 33, 2852 (1968).

12. M. Schenck, Ber., 75, 198 (1942).

13. M. Schenck, Ber., 76, 874 (1943).

14. M. Schenck, Ber., 77B, 29 (1944).

15. A. Angeli and E. Rimini, Ber., 28, 1077 (1895).

16. A. Hantzsch and F.E. Dollfus, Ber., 35, 260 (1902).

17. J.F. Brown Jr., Abstracts of Papers, 126th Meeting, American Chem. Soc., Sept. 12-17, p. 43-O (1954).

18. T. Wieland and D. Grimm, Chem. Ber., 96, 275 (1963).

19. G.S. Hammond, "Steric Effects in Organic Chemistry", M.S. Newman Ed., Wiley, New York, N.Y., p. 468 (1956).

20. St. Goldschmidt and D.L.C. Veer, Rec. Trav. Chim. Pays-Bas, 65, 796 (1940); 66, 238 (1947).

21 (a) J.P. Freeman, Chem. Rev., 73, 283 (1973); (b) J.M. Kliegman and R.K. Barnes, J. Org. Chem., 37, 4223 (1972).

22. J.P. Freeman, J. Org. Chem., 26, 4190 (1961).

23. A. Angeli and E. Rimini, Gazz. Chim. Ital., 26, II, 34 (1896).

24. O. Angelucci, Annalen, 341, 172 (1905).

25. R. Fusco and G. Trisoglio, Atti. Accad. Lincei, Rend., Cl. Sci Fis., Mat. Natur., [7]2, 618, 751 (1941).

26. J.P. Freeman, J. Org. Chem., 27, 1309 (1962).

27. R. Scholl, Annalen, 338, 1 (1905).

28. J.W. Suggett, G.S. Meyers and G.F. Wright, J. Org. Chem. 12, 373 (1947).

29. S.G. Brooks, R.M. Evans, G.F.H. Green, J.S. Hunt, A.G. Long, B. Mooney and L.J. Wyman, J. Chem. Soc., 4614 (1958).

30. J.P. Freeman, Chem. and Ind., 1624 (1960).

31. L.J. Bellamy, "The IR spectra of complex Molecules". John-Wiley & Sons, Inc., New York, N.Y., p. 269 (1959).

32. Ref. 31, p. 304.

33. R. Bonnett, R.F.C. Brown, V.M. Clark, I.O. Sutherland and A. Todd, J. Chem. Soc., 2094 (1959).

34. R.N. Haszeldine and J. Jander, J. Chem. Soc. 691 (1954).

35. W. Baker and W.D. Ollis, Quart, Revs., 11, 15 (1957).

36. G.A. Boswell Jr., J. Org. Chem., 33, 3699 (1968).

37. J. Houben and E. Pfankuch, Ber. Dtsch. Chem. Ges., 60, 586 (1927).

38. G. Buchi and H. Wuest, J. Org. Chem, 44, 4116 (1979).

39. T. Matsumoto and S. Yasuda, Tetrahedron Lett., 5311 (1968).

40. L. Horner, L. Hockenberger and W. Kirmse, Chem. Ber., 94 290 (1961).

41. A. Gandini, Gazz. Chim. Ital. 72,232 (1942).

42. D.H.R. Barton, P.G. Sammes and M. Silva, Tetrahedron, Suppl., 57 (1966).

43. R. Scholl, Ber., 21, 506 (1888).

44. J.P. Freeman and J.J. Gannon, J. Org. Chem., 34, 194 (1969).

45. J.P. Freeman and J.F. Hansen, J. Chem. Soc., Chem. Commun., 961 (1972).

46. N. Mangelli, G. Modena and P.E. Todesco, Gazz. Chim. Ital., 90, 1 (1969).

47. D. Barnerd and E.J. Percy, Chem. and Ind., 1332 (1960).

48. J.L. Riebsomer, Chem. Rev., 36, 157 (1945).

49. M.M. Frojmovic and G. Just, Can. J. Chem., 46, 3719 (1968).

50. B.C. Gilbert and R.O.C. Norman, J. Chem. Soc., B, 86 (1966).

51. J.H. Boyer, "The Chemistry of Nitro and Nitroso Group", H. Feur. Ed., Interscience, New York, N.Y., p. 235 (1969).

52. M.J. Danzing, R.F. Martel and S.R. Riccitello, J. Org. Chem., 26, 3327 (1961).

53. O.L. Chapman and D.C. Heckert, J. Chem. Soc., Chem. Commun., 242 (1966).

54. P.A.S. Smith, "Open Chain Nitrogen Compounds", Vol. 2, W.A. Benjamin, New York, N.Y., p. 57 (1966).

55. Ch. Forster, W. Kiessling, M. Lubing, W. Pritzkow and P. Radloff, J. Prakt. Chem., 311, 370 (1969).

56. C.G. Francisco, D. Melian, J.A. Salazar and E. Suarez, J. Chem. Soc., Perkin I, 923 (1982).

57. C.G. Francisco, R. Freire, R. Hernandez, D. Melian, J.A. Salazar and E. Suarez, J. Chem. Soc., Perkin I, 297 (1983).

58. A. Angeli, Atti Accad. Lincei, [5]4, II, 255 (1895).

59. A. Hantzsch and F.E. Dollfus, Ber. Dtsch. Chem. Ges., 26, 226 (1902).

60. Sukh Dev, Tetrahedron, 9, 1 (1960).

61. A. Angeli and V. Castellane, Atti. Accad. Lincei, [5]14, I, 669 (1905).

62. W. Steglic and G. Hofie, Angew. Chem. Int. Ed. Eng., 8, 981 (1969).

63. W. Jagar, Methoden Org. Chem. (Houben-Weyl), 5/2a, 33 (1977).

64. G. Kobrich and P. Buck, Chem. Acetylenes, 99 (1969).

65. J.B. Hendrickson and J.R. Sufrin, Tetrahedron Lett., 1513 (1973).

66. A. Gandini, Gazz. Chim. Ital., 72, 131 (1942).

67. L.J. Winters, J.F. Fischer and E.R. Ryan, Tetrahedron Lett., 129 (1971).

68. T. Sato and H. Obase, Tetrahedron Lett., 1633 (1967).

69. J. Baldwin, "Experimental Organic Chemistry", McGraw-Hill, New York, N.Y. p. 100 (1965).

70. W.C. Agosta and D.K. Herron, J. Am. Chem. Soc., 90, 7025 (1968).

71. H. Feur and P.M. Pivawar, J. Org. Chem., 31, 3152 (1966).

72. A.T. Nielson, Chem. Nitro. Nitroso Groups, 349 (1969).

73. R.T. Aplin, M. Fischer, D. Becher, H. Budzikiewicz and C. Djerassi, J. Am. Chem. Soc., 87, 4888 (1965).

74. L. D' Or and J. Collin, Bull. Soc. Roy. Sci. Liege, 285 (1953).

75. H. Budzikiewicz, C. Djerassi and H. Williams, "Interpretation of Mass spectra of Organic Compounds", Holden-Day, Inc., San Fransisco, Calif., Chapter 1-6 (1964).

76. N.M.M. Nibbig, Th. J. de Boer and J.H. Hofman, Rec. trav. Chim., 84, 481 (1965).

77. J. Momigny, Bull. Soc. Roy Sci. Liege, 25, 93 (1956)

78. J.H. Beynon, R.A. Saunders and A.E. Williams, Ind. Chim., Belge., 29, 311 (1964).

79. M.M. Bursey and F.W. McLafferty, J. Am. Chem. Soc., 88, 5023 (1966).

80. J.H. Beynon, G.R. Laster and A.E. Williams, J. Phys. Chem., 63, 1861 (1959).

81. R.A. Saunders and A.E. Williams, "Mass Spectrometry of Organic Ions", F.W. McLafferty, Ed., Academic Pres , New York, N.Y., p. 376 (1963).

82. J.H. Beynon, "Mass Spectrometry and Its Application to Organic Chemistry", Elsevier, Amsterdam. p. 268 (1960)

83. S. Meyerson, I. Puskas and E.K. Fields, J. Am. Chem. Soc., 88, 4974 (1966).

84. G. Spiteller, Montash, 92, 1147 (1961).

85. D.P. Stevenson and C.D. Wagner, J. Chem. Phys., 19, 11 (1951).

86. D.P. Stevenson, J. Chem. Phys., 19, 17 (1951).

87. J.H. Beynon, R.A. Saunders, A. Topham and A.E. Williams, J. Chem. Soc., 6403 (1965).

88. Ref. 73, p. 191.

89. G. Ciamiccian and P. Silber, Ber., 34, 2040 (1901).

90. J.H. Bowie, D.W. Cameron and D.H. Williams, J. Am. Chem. Soc., 87, 5094 (1965).

91. J.H. Mason, T.P. Toube and D.H. Williams, J. Chem. Soc., B, 396 (1966).

92. J.H. Beynon, B.E. Job and A.E. Williams, Z. Naturf, 21a, 210, (1966).

93. T. Aczel and H.E. Lupkin, Anal. Chem., 32, 1819 (1960).

94. J.T. Pinhey and E. Rizzardo, Chem. Commun., 362 (1965).

95. T.H. Kinstle, J.R. Althaus, J.G. Stam and J.P. Bechner, J. Org. Chem, (In press); Ref. 75, p.519.

96. E. Bamberger, Ber., 51, 606 (1918).

97. T.H. Kinstle and J.G. Stam, J. Org. Chem., 35, 1771 (1970).

98. O.L. Chapman, P.G. Cleveland and E.D. Hoganson, J. Chem. Soc. Chem. Commun. 101 (1966).

99. C.W. Shoppee, R.E. Lack and S.K. Roy, J. Chem. Soc., 3767 (1963).

100. D.N. Jones, J.R. Lewis, C.W. Shoppee and G.H.R. Summers, J. Chem. Soc., 2876 (1955).

101. E.G. Ford, P. Chakarvorty and E.S. Wallis, J. Am. Chem. Soc., 60, 413 (1938).

102. C.W. Shoppee and G.H.R. Summers, J. Chem. Soc., 1786 (1952).

103. L. Knoff, Annalen, 642, 194 (1961).

104. R.M. Dodson and B. Riegel, J. Org. Chem., 13, 424 (1948).

105. E.S. Wallis, E. Fernholz and F.T. Gephart, J. Am. Chem. Soc., 59, 137 (1937).

106. I.M. Heilbron, J. Hodges and F.S. Spring, J. Chem. Soc., 759 (1938).

107. C.W. Shoppee, G. Krugar and R.N. Mirrington, J. Chem. Soc., 1050 (1962).

108. R.H. Mazur, J. Org. Chem., 28, 248 (1963).

109. R.M. Silverstein, G.C. Bassler and T.C. Morrill, "Spectometric Identification of Organic Compounds", John Wiley & Sons, New York, page 220 (1981).

110. L.F. Fieser, J. Am. Chem. Soc., 75, 5421 (1953).

111. C.W. Shoppee, M.I. Akhtar and R.E. Lack, J. Chem. Soc., 3388 (1964).

112. W.G. Dauben and K.H. Takemura, J. Am. Chem. Soc., 75, 6302 (1953).

113. M.S. Ahmad, Shafiullah and Islamuddin, Ind. J. Chem., B, 12, 1323 (1974).

114. O.R. Peterson and C.T. Chen, J. Am. Chem. Soc., 77, 2557 (1955).

115. A.H. Milburn and E.V. Truter, J. Chem. Soc., 1736 (1956).

116. H.J. Eckhardt, Ber., 71, 461 (1938).

117. W.G. Dauben and G.J. Fonken, J. Am. Chem. Soc., 78, 4736 (1956).

118. I.M. Heilbron, E.R.H. Jones and F.S. Spring, J. Chem. Soc, 1736 (1956).

119. J. Jander and R.N. Haszeldine, J. Chem. Soc., 919 (1954).

120. D.H. Williams and I. Fleming, "Spectromeric Methods in Organic Chemistry", McGraw Hill Phublishing Co. Ltd., London, p. 65 (1966).

121. C.E. Anagnostopoulos and L.F. Fieser, J. Am. Chem. Soc, 76, 532 (1954).

122. L.F. Fieser and M. Fieser, Steroids, Reinhold, New York, p. 28 (1959).

123. H.C. Brown and P.J. Geoghegan Jr., J. Org. Chem., 35, 1844 (1970).

124. H.C. Brown, P.J. Geoghegan Jr., J.T. Kurek and G. J. Lynch, Organometal. Chem. Synth., 1, 7 (1970/1971).

125. H.C. Brown, P.G. Geoghegan Jr., G.J. Lynch and J.T. Kurek, J. Org. Chem., 37, 1941 (1972).

126. D.J. Pasto and J.A. Gontarz, J. Am. Chem. Soc., 93, 6902 (1971).

127. H.C. Brown, G.J. Lynch, W.J. Hammar and L.C. Liu, J. Org. Chem., 44, 1910 (1979).

128. A. Factor and T.G. Traylor, J. Org. Chem., 33, 2607 (1968).

129. T.T. Tidwell and T.G. Traylor, J. Org. Chem., 33, 2614 (1968).

130. T.G. Traylor and A.W. Baker, J. Am. Chem. Soc., 85, 2746 (1963).

131. K.C. Pande and S. Winstein, Tetrahedron Lett., 3393 (1964).

132. J.K. Stille and S.C. Stinson, Tetrahedron, 20, 1387 (1964).

133. M.M. Anderson and P.M. Henry, Chem. and Ind. (London), 2053 (1961).

134. T.G. Traylor, J. Am. Chem. Soc., 86, 244 (1964).

135. K.A. Hofmann and J. Sand, Chem. Ber., 33, 1340 (1900).

136. P. Karrer and C.H. Eugster, Helv. Chim. Acta., 34, 1400 (1951).

137. H. Inhoffen and W. Arend, Annalen, 578, 177 (1952).

138. W. Triebs, G. Lucius, H. Kogler and H. Breslauer, Annalen, 581, 59 (1953).

139. D.H.R. Barton and W.J. Rosenfelder, J. Chem. Soc., 2381 (1951).

140. J.C. Strini and J. Metzger, Bull. Soc. Chim. France, 3150 (1966).

141. M.S. Ahmad, Shafiullah and S.C. Logani, Aust. J. Chem., 21, 1909 (1968).

142. M.S. Ahmad, S.C. Logani and G.A.S. Ansari, Ind. J. Chem., B, 9, 1329 (1971).

143. M.S. Ahmad and S.C. Logani, Aust. J. Chem., [illegible] 43 (1971).

144. G.A. S. Ansari, Ph.D. Thesis, A.M.U., Aligarh (1972).

145. C.W. Shoppee and G.H.R. Summers, J. Chem. Soc., 3361 (1952).

146. H. Reich, F.E. Walker and R.W. Collins, J. Org. Chem., 16, 1753 (1951).

147. L.F. Fieser and M. Fieser, "Steroids", Reinhold, New York, p.1 (1959).

148. C.E. Anagnostopoulos and L.F. Fieser, J. Am. Chem. Soc., 83, 4249 (1961).

149. M.S. Ahmad and A.H. Siddiqui, J. Ind. Chem. Soc., 46, 44 A. (1969).

150. I.K. Kaye, U. Weiss and R.J. Highet, Steroids, 8(1), 1 (1966).

151. L.F. Fieser and M. Fieser, "Steroids", Reinhold, New York, p. 43-44 (1959).

152. J.R. Bull, E.R.H. Jones and G.D. Meakins, J. Chem. Soc., 2601 (1965).

153. N.F. Blau and C.G. Stuckwisch, J. Org. Chem., 27, 370 (1962).

154. J. Collins, Bull. Soc. Roy. Liege, 25, 426 (1956).

155. G.D. McDonald, J.S. Shannon and G. Sugowdz, Tetrahedron Lett., 807 (1963).

156. R.H. Baker and E.N. Squire, J. Am. Chem. Soc., 70, 1487 (1948).

157. M.Z. Alam, M.Phil. Dissertation, A.M.U. Aligarh (1983).

158. I.M. Heilbron, E.R.H. Jones and F.S. Spring, J. Chem. Soc., 801 (1937).